REMARKS/ARGUMENTS

Status of Claims

Claims 31, 32, 34, and 36-37 are pending and are under examination. Claims 1-30, 33, and 35 are cancelled.

Amendments to the Claims

No amendments to the claims were made.

Priority of Claims 31, 32, 34, and 36-37

This application claims benefit of U.S. provisional application no. 60/491,350 ("350 Application"), filed July 31, 2003 and claims benefit of U.S. provisional application no 60/509,037 ("'037 Application") filed October 4, 2002 (converted from non-provisional application no. 10/264,825).

Sequence Compliance

Applicants acknowledge the Examiner's withdrawal of the objection to the sequence listing.

Specification

Applicants acknowledge the Examiner's withdrawal of the objection to the specification.

Withdrawal of Rejections

Applicants acknowledge the Examiner's withdrawal of the rejections made under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 112, first paragraph. As such, the instant application provides written description and enablement for pending claims 31, 32, 34, and 36-37.

Drawings

The Examiner did not acknowledge the drawings which were originally filed. Specifically, the Examiner did not indicate in the Office Actions mailed August 22, 2006 and May 1, 2007 whether the drawings submitted by Applicants were accepted or objected to by the Examiner. Applicants respectfully request acknowledgement of the acceptance of the drawings or objection by checking the appropriate box in the next Office Action.

Applicants' Invention

Applicants discovered that cancer cells overexpress a protein, Dvl-3, and that inhibiting expression of Dvl-3 inhibits the growth of cancer cells overexpressing Dvl-3. Nothing in the prior art suggested this invention.

Claim Rejection - 35 USC § 102(b)

The Examiner rejected Claims 31 and 37 under 35 U.S.C. § 102(b) as being anticipated by Song *et al.* (*J. Biol. Chem.* 275:23790-23797 (2000); "Song"). According to the Examiner, Song teaches that (i) protein kinase CK2 is involved in tumorigenesis (p. 23790, col. 2), (ii) CK2 is important to modulate phosphorylation of Dvl-3 which is expressed in breast cancer cells because when breast cancer cells were treated with apigenin, a CK2 inhibitor, the phosphorylation of Dvl-3 protein is diminished (Figure 5), (iii) apigenin reduces the levels of Dvl-3 protein in breast cells, and (iv) apigenin inhibits cell proliferation.

The rejection is respectfully traversed.

A. *The Legal Standard*

For a rejection of claims under §102 to be properly founded, the Examiner must establish that a single prior art reference either expressly or inherently discloses each and every element of the claimed invention. *See, e.g. Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986), *cert denied*, 480 U.S. 947 (1987); and *Verdegaal Bros. V. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). In *Scripps Clinic & Research Found. V. Genentech, Inc.*, 18 USPQ2d 1001 (Fed. Cir. 1991), the Federal Circuit held that:

> "Invalidity for anticipation requires that **all of the elements and limitations** of the claim are found **within a single prior art reference**.... There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Id.* at 1010.

Anticipation cannot be found, therefore, unless a cited reference discloses all of the elements, features or limitations of the presently claimed invention. Applicants respectfully submit that Song fails to recite all of the elements of claims 31 and 37.

B. ***Song Does Not Disclose A Cancer Cell That Overexpresses A Dvl-3 Protein And Does Not Disclose An Agent That Inhibits Dvl-3 Expression***

The Examiner acknowledged that nowhere does Song teach a cancer cell (claim 31) or a breast cancer cell (claim 37) *overexpressing* a Dvl-3 protein. Song does not compare a normal cell and a cancer cell or a normal cell and a breast cancer cell to determine that the cancer cell or breast cancer cell overexpresses a Dvl-3 protein. Further, Applicants submit that, contrary to the Examiner's allegation, Figure 5 of Song does not show that apigenin, an inhibitor of CK2, diminishes phosphorylation of Dvl-3. Only Figure 5B reports an experiment using apigenin and this particular experiment refers to the diminished phosphorylation of β-catenin, not Dvl-3 (Figure 5B).

Song does not teach or suggest an agent that inhibits Dvl-3 *expression.* Song teaches that apigenin, an inhibitor of CK2, through an unknown mechanism, causes the degradation of a Dvl-3 protein that *already exists* in a cell. Song does not teach or suggest that apigenin inhibits Dvl-3 *expression* (i.e., transcription of a Dvl-3 mRNA from a Dvl-3 encoding gene or translation of the Dvl-3 mRNA to produce a Dvl-3 protein, as one of ordinary skill in the art would understand the term "expression" in the context of Applicants' claims). Song states on page 23795, col. 1 in the context of Figures 6 and 7:

> "To determine whether the reduction in β-catenin occurred through a decreased rate of synthesis or increased rate of degradation, we measured the half-life of the protein in the presence of a *cycloheximide* that blocked new protein synthesis. We found that β-catenin is quite stable in Wnt-1-expressing cells, with a half-life of more than 5 h (Fig. 7) ... The *Dvl*

> *proteins* appear to be equally stable. However, in the presence of apigenin, protein levels rapidly decline. *Immunoreactive Dvl proteins disappears* in less than 30 min..." (emphasis added)

Because cycloheximide is a protein synthesis inhibitor that acts specifically on the 60S subunit of eukaryotic ribosomes, Song investigated the effect of apigenin *on already expressed* Dvl-3 protein and did not investigate the effect of an agent that inhibited the expression of Dvl-3 protein.

Claims 31 and 37 require an agent that inhibit the *expression* of a Dvl-3 protein. Song does not teach or suggest all limitations of claims 31 and 37. Therefore, Song does not anticipate claims 31 and 37.

Applicants respectfully request withdrawal of the rejection of these claims under 35 U.S.C. § 102(b).

Claim Rejection - 35 USC § 102(e)

The Examiner rejected Claims 31, 32, 34, and 37 under 35 U.S.C. § 102(e) as being anticipated by Alsobrook *et al.* (US 20030229016 based on U.S. Application Ser. No. 10/307,928 ("'928 Application"), filed December 2, 2002 and published December 11, 2003; priority to 8/26/02 and earlier; "Alsobrook"). According to the Examiner, Alsobrook teaches methods for treating a cancer cell such as a lung cancer cell or breast cancer cell [0016] using an siRNA [0080] which inhibits expression of a splice variant of a dishevelled-3-like protein (Table 1). The Examiner appreciated that Applicants' claims are not limited to any kind of Dvl-3 protein moiety and argued that Alsobrook's disclosure of the use of the splice variant for a Dvl-3 like protein for inhibiting the expression of the Dvl-3 like protein to inhibit cancer cell proliferation (i.e., using siRNA as an agent) anticipates Applicants' claims 31, 32, 34, and 37.

The rejection is respectfully traversed.

A. *The Legal Standard*

The legal standard for a rejection of claims under §102 is discussed *supra.*

B. ***None Of The Alsobrook Earlier Filed Provisional Patent Applications Disclose The Subject Matter Of Applicants' Claims***

Alsobrook was filed as U.S. Application Ser. No. 10/307,928 ("'928 Application") on December 2, 2002, claiming priority to eleven (11) provisional patent applications, including:

(1) 60/406,353 ("'353 Application"), filed August 26, 2002;

(2) 60/401,788 ("'788 Application"), filed August 7, 2002;

(3) 60/384,024 ("'024 Application"), filed May 29, 2002;

(4) 60/383,744 ("'744 Application"), filed May 28, 2002;

(5) 60/381,495 ("'495 Application"), filed May 17, 2002;

(6) 60/380,981 ("'981 Application"), filed May 15, 2002;

(7) 60/373,288 ("'288 Application"), filed April 17, 2002;

(8) 60/344,903 ("'903 Application"), filed December 31, 2001;

(9) 60/342,592 ("'592 Application"), filed December 20, 2001;

(10) 60/341,540 ("'540 Application"), filed December 17, 2001; and

(11) 60/341,477 ("'477 Application"), filed December 17, 2001, collectively referred to as "Alsobrook provisional applications."

To the extent that these Alsobrook provisional applications were available on PAIR for Applicants' review, Applicants submit that none of these Alsobrook provisional applications teaches a method for treating a cancer cell (such as a lung cancer or breast cancer cell) that *overexpresses* a Dvl-3 protein by contacting the cell with an agent (such as a siRNA) that inhibits Dvl-3 expression wherein the growth of the cancer cell is inhibited.

None of the '353, '788, '024, '744, '495, '981, '288, '592, '540, and '477 Applications disclose the Dvl-3 splice variant. The '903 Application, filed on December 31, 2001, discloses on pages 53 to 79 a Dvl-3 splice variant which is also disclosed in Alsobrook's '928 Application. The remainder of the '903 Application, however, includes disclosure which is unrelated to Dvl-3, but rather discloses proteins and nucleic acids for Colonic And Hepatic Tumor Over-Expressed Protein-like Proteins, Acetyltransferase-like Proteins, Granzyme H-like Proteins, Fibulin-2-like Proteins, 4930418P06RIK Rhomboid-like Proteins, DORA Protein Precursor-like Proteins, IPAS-like Proteins, splice variants of Cartilage Oligomeric Matrix

Protein-like Proteins, and splice variants of Insulin-like Growth Factor Binding Protein 4 (IGFBP4)-like Proteins.

Pages 53 to 79 of the '903 Application are provided for the Examiner's review as **Exhibit A**. Applicants submit that with respect to the disclosure of the Dvl-3 splice variant, the '903 Application discloses various sequence alignments, hydropathy data (Figures 1-5), and tissue expression data of Dvl-3 (page 59). Specifically, with respect to expression of the Dvl-3 splice variant, the '903 Application discloses expression of the Dvl-3 splice form in various normal tissues and two tumors (ovary and parathyroid gland) (page 59).

Applicants submit that the '903 Application, however, does not disclose all limitations of Applicants' claims 31, 32, 34, and 37. For example, the '903 Application does not teach *overexpression* of the Dvl-3-like protein in any cancer cell, such as a lung cancer cell or breast cancer cell. In fact, the '903 Application does not even mention lung cancer or breast cancer. The '903 Application does also not disclose an agent, such as an siRNA, for the inhibition of Dvl-3 expression.

As such, Alsobrook is not entitled to benefit of the priority date of the '903 Application for allegedly disclosing Applicants' subject matter of claims 31, 32, 34, and 37.

Because none of the other Alsobrook provisional applications provides the a disclosure of the Dvl-3 splice variant, Alsobrook is also not entitled to claim benefit of any of these Alsobrook provisional patent applications for the alleged disclosure of the subject matter of Applicants' claims 31, 32, 34, and 37.

As such, in rejecting claims 31, 32, 34, and 37 under 102(e) as allegedly being anticipated by Alsobrook, the Examiner must rely on the disclosure of the '928 Application, which has a filing date of December 2, 2002.

C. ***Alsobrook's '928 Application Does Not Qualify As Prior Art Under 35 U.S.C. § 102(e)***

The presently examined application claims benefit of U.S. Provisional Application No. 60/509,037 ("'037 Application") filed October 4, 2002. This filing date predates the filing date of Alsobrook's '928 Application by two months. Specifically, Applicants' claim

31 is supported by the '037 Application (see, for example, page 17, lines 20-21; page 36, lines 23-24; page 37, lines 29-32, page 38, lines 10-15, page 38, lines 20-21; Figure 9). Therefore, the '928 Application does not qualify as prior art under 35 U.S.C. § 102(e) and the rejection of claim 31 should be withdrawn. Claims 32, 34, and 37 depend on claim 31 and incorporate the limitations of claim 31. Thus, Alsobrook is also not prior art against dependent claims 32, 34, and 37.

Applicants respectfully request withdrawal of the rejection of claims 31, 32, 34, and 37 under 35 U.S.C. § 102(e).

D. *Alsobrook's '928 Application Does Not Disclose A Cancer Cell That Overexpresses A Dvl-3 Protein*

As discussed above, the only potentially relevant Alsobrook application is the '928 Application. Applicants submit that the '928 Application does not anticipate Applicants' claims because it does not teach all of the limitations of the claims.

Alsobrook does not teach or suggest a cancer cell (claims 31, 34), a lung cancer cell (claim 32), or a breast cancer cell (claim 37) *overexpressing* a Dvl-3 protein. Thus, Alsobrook does not teach the limitation of Applicants' claim "a cancer cell that overexpresses a Dvl-3 protein." As such Alsobrook does not teach all limitations of Applicants' claims and it is an improper §102 reference.

Applicants respectfully request withdrawal of the rejection of claims 31, 32, 34, and 37 under 35 U.S.C. § 102(e).

E. *Applicants' Invention Predates Alsobrook's '928 Application*

The Alsobrook '928 Application is cited by the Examiner as a 102(e) reference. It is, thus, subject to swearing behind. Accordingly, without conceding that Alsobrook's '928 Application provides an enabling disclosure of each and every element and limitation for the subject matter of Applicants' claims 31, 32, 34, and 37, Applicants herewith submit a Declaration under 37 CFR 1.131 which establishes that Applicants completed their invention prior to the effective filing date of Alsobrook's '928 Application, which is December 2. 2002. Evidence of

Applicants' conception of the invention prior to December 2, 2002 includes (i) the finding that tumor cells when compared to normal cells overexpress Dvl-3 mRNA; (ii) the finding that cancer cells, including lung cancer cells, breast cancer cells and mesothelioma, overexpress a Dvl-3 protein when compared to normal or non-tumor cells; (iii) designing Dvl-3 siRNA nucleic acids for inhibition of Dvl-3 expression; and (iv) ordering Dvl-3 siRNA nucleic acids for inhibition of Dvl-3 expression. After conceiving of the invention, Applicants diligently worked towards actual and constructive reduction to practice their invention.

In view of the arguments provided herein and further in view of the Rule 131 Declaration, Alsobrook is not longer considered anticipatory art. Applicants submit that the rejection of claims 331, 32, 34, and 47 over Alsobrook has been fully addressed. Reconsideration and withdrawal of this reference as a basis for the 35 U.S.C. §102(e) rejection is respectfully requested.

Claim Rejection - 35 USC § 103(a)

A. *The Legal Standard*

Establishing a *prima facie* case for obviousness under § 103 requires the Examiner show, *inter alia*:

(1) The prior art references teach or suggest all claim limitations of the rejected claim(s). *In re Royka*, 180 USPQ 580 (CCPA 1974); and MPEP §2143.03.

(2) The existence of some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir., 1988).

(3) A reasonable expectation of success in combining the references. This must be found in the prior art, and not in the applicants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir., 1991).

A *prima facie* case of obviousness requires the Examiner to provide an explicit reason why one of ordinary skill in the art would combine the known elements in the fashion claimed by Applicants. Recently, in reviewing this standard, the Supreme Court noted that any

analysis supporting a rejection under § 103(a) must be made explicit, and that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements in the manner claimed. *KSR Intl Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (U.S. 2007). "This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *Id.* To support a rejection under § 103 using the Federal Circuit's teaching-suggestion-motivation (TSM) test, the Office must provide evidence that demonstrates some suggestion or motivation to modify or combine the references, whether in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine* 837 F.2d at 1074, MPEP § 2143.

A *prima facie* case of obviousness requires the Examiner to show that one of ordinary skill in the art would have had a reasonable expectation of success in modifying the prior art references, or in combining their relevant teachings. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir., 1991). The teaching or suggestion to make the claimed combination *and* the reasonable expectation of success must both be found in the prior art, and *not* based on applicant's disclosure. *Id.* The Examiner's suggestion of the desirability of doing what the inventor has done must be found either expressly or impliedly in the references, or supported by a convincing line of reasoning, which must rely on logic and sound scientific reasoning. *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). *See also* MPEP § 2144; and *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993) (requiring reliance on logic and sound scientific reasoning in supporting a conclusion of obviousness).

B. ***Rejection of Claims 31 and 37 Over Song and Bui***

The Examiner rejected Claims 31 and 37 under 35 U.S.C. § 103(a) as being unpatentable over Song further in view of Bui *et al.* (*Biochem. Biophys. Res. Comm.* 239:510-516 (1997); "Bui"). According to the Examiner, a method of inhibiting the growth of a cancer cell, such as a breast cancer cell, with an agent that effects Dvl-3 expression was *prima facie* obvious at the time of the invention over Song and Bui. The Examiner acknowledged that Song does not teach Dvl-3 expression in cancer cells and cites to Bui to provide this teaching.

The rejection is respectfully traversed.

1. *The Combination Of Song And Bui Fails To Teach All Elements Of the Applicants' Invention*

The teaching of Song has been discussed in detail *supra*. As also acknowledged by the Examiner (page 8 of the Office Action), Song does not disclose a cancer cell that expresses or overexpresses a Dvl-3 Protein. Further, as discussed *supra*, Song does not disclose an agent that inhibits Dvl-3 expression.

Bui merely discloses Dvl-3 expression in various cancer cell lines, including breast cancer cells, but does not disclose "an agent that inhibits Dvl-3 expression." As such, neither Song nor Bui disclose "an agent that inhibits Dvl-3 expression to inhibit the growth of a cancer cell." Bui cannot provide the missing claim element and claim limitation that is also missing in Song. Therefore, the combination of Song and Bui does not disclose all elements and all claim limitations of Applicants' claims 31 and 37.

As the combination of references suggested in the Office Action *fails to provide all of the elements* of Applicants' claimed invention, a *prima facie* case of obviousness has not been set forth. Therefore, Applicants respectfully request the rejection of claims 31 and 37 be withdrawn.

2. *Bui Teaches Away From Applicants' Invention, There Is No Motivation To Make The Suggested Combination And No Reasonable Expectation Of Success*

Because Bui teaches that Dvl-3 is not overexpressed in cancer cells, it provides a reason against combination with Song. Therefore, one of ordinary skill in the art would not be motivated to combine the Song and Bui references. Specifically, Bui teaches in the abstract that:

> "Statistically, there was no difference in DVL-3 mRNA level between normal breast tissues and tumors. In human colorectal samples, DVL-3 was expressed equally in matched normal tissues, polyps and tumors." (Emphasis added).

and on page 515, column 1:

> "We have also investigated a potential role for DVL-3 in human breast and colon tumorigenesis ... Since the Wnt gene is an upstream signal of

> DVL in the wingless signaling pathway, it was thought that aberrant expression of Wnt could alter DVL expression. However, the data presented here showed no difference in DVL-3 mRNA expression between normal breast tissues and corresponding tumours, and between matched normal colon tissues, polyps and tumors." (Emphasis added).

This is directly opposed to Applicants' discovery and claimed invention. Contrary to Bui's teaching, Applicants' invention requires a cancer cell to *overexpress* a Dvl-3 protein. Bui expressly teaches away from Applicants' invention. Teaching away is a strong motivation for one of ordinary skill in the art to not combine references and has been acknowledged to be strong evidence for the invention in question to be not obvious. Because of Bui's teaching away, there can also be no reasonable expectation of success in combining the Song and Bui references. The reasonable expectation of success must be found in the prior art, and not in the Applicants' disclosure.

As the references suggested in the Office Action *fail to motivate to make the suggested combination* of Applicants' claimed invention and *fail to provide a reasonable expectation of success*, Applicants' invention cannot be obvious in view of the cited art. A *prima facie* case of obviousness has not been set forth. Therefore, Applicants respectfully request the rejection of Claims 31 and 37 under 35 U.S.C § 103(a) be withdrawn.

C. *Rejection of Claims 31 and 32 Over Song and Engelmann*

The Examiner rejected Claims 31 and 32 under 35 U.S.C. § 103(a) as being unpatentable over Song further in view of Engelmann *et al.* (*Phytomedicine* 9(6):489-495 (2202); "Engelmann"). According to the Examiner, a method of inhibiting a lung cancer cell with an agent that effects Dvl-3 expression was *prima facie* obvious at the time of the invention over Song and Engelmann. The Examiner acknowledged that Song does not teach using the method of inhibiting cancer cell growth in a lung cancer cell and cites to Engelmann to provide this teaching.

The rejection is respectfully traversed.

1. *The Combination Of Song And Engelmann Fails To Teach All Elements Of the Applicants' Invention*

The teaching of Song has been discussed in detail *supra*. As acknowledged by the Examiner (page 8 of the Office Action), Song does not disclose a cancer cell that expresses or overexpresses a Dvl-3 Protein (claim 31) or using the method of inhibiting growth of a lung cancer cell (claim 32) (page 9 of the Office Action). Further, as discussed *supra*, Song does not disclose an agent that inhibits Dvl-3 expression.

According to the Examiner, Engelmann discloses in the abstract inhibition of lung cancer, glioma and colon cancer in vivo with apigenin.

As discussed *supra* and as acknowledged by the Examiner, apigenin is an inhibitor of CK2. While apigenin may or may not have a direct or indirect effect on Dvl-3 protein levels or protein stability as alleged by the Examiner, both Song and Engelmann references fail to provide evidence that apigenin is an agent that inhibits Dvl-3 *expression*. As such, both references taken individually or combined fail to provide an agent that inhibits Dvl-3 expression as required by Applicants' Claims 31 and 32.

As the combination of references suggested in the Office Action *fails to provide all of the elements* of Applicants' claimed invention, a *prima facie* case of obviousness has not been set forth. Therefore, Applicants respectfully request the rejection of Claims 31 and 32 be withdrawn.

2. *There Is No Motivation To Make The Suggested Combination And No Reasonable Expectation Of Success*

There is nothing in Engelmann that would lead one of ordinary skill in the art make believe that the teaching of Engelmann would be useful for inhibiting Dvl-3 expression. Engelmann does not even mention Dvl-3. Therefore, one of ordinary skill in the art would not be motivated to combine the teaching of Song and Engelmann.

As the references suggested in the Office Action *fail to motivate to make the suggested combination* of Applicants' claimed invention and *fail to provide a reasonable expectation of success*, Applicants' invention cannot be obvious in view of the cited art. A *prima*

facie case of obviousness has not been set forth. Therefore, Applicants respectfully request the rejection of Claims 31 and 32 under 35 U.S.C § 103(a) be withdrawn.

D. ***Rejection Of Claims 31 and 36 Over Song And You As Evidenced By Uematsu***

The Examiner rejected Claims 31 and 36 under 35 U.S.C. § 103(a) as being unpatentable over Song further in view of You *et al.* (*Proc. Am. Assoc. Cancer Res.* 42:609 (2001); "You") as evidenced by Uematsu *et al.* (*Oncogene* 22:7218-7221 (2003); "Uematsu"). According to the Examiner, a method of inhibiting a mesothelioma cell with an agent that effects Dvl-3 expression was *prima facie* obvious at the time of the invention over Song and You as evidenced by Uematsu. The Examiner acknowledged that Song does not teach using the method of inhibiting cancer cell growth in a mesothelioma and cites to You to provide this teaching.

The rejection is respectfully traversed.

1. ***The Combination Of Song And You Fails To Teach All Elements Of the Applicants' Invention***

The teaching of Song has been discussed in detail *supra.* As acknowledged by the Examiner (page 8 of the Office Action), Song does not disclose a cancer cell that expresses or overexpresses a Dvl-3 Protein (claim 31) or using the method of inhibiting growth of a mesothelioma (claim 36) (page 10 of the Office Action). Further, as discussed *supra,* Song does not disclose an agent that inhibits Dvl-3 expression.

According to the Examiner, You discloses in the abstract overexpression of Dvl and its apparent involvement in inducing tumorigenicity by a canonical Wnt signaling pathway.

As the Examiner is aware, Dvl proteins include Dvl-1, Dvl-2, and Dvl-3 proteins. Applicants submit that while You discloses that a Dvl protein is overexpressed in mesothelioma cells, the abstract by You does not disclose that the Dvl protein is Dvl-3 as required by Applicants' claims. Later experiments, e.g., those disclosed in Applicants' '037 Application showed that the Dvl protein overexpressed in mesothelioma cells, as described by You, includes a Dvl-3 protein.

Further, and more importantly, You does not teach an agent that inhibits Dvl-3 expression (or Dvl expression) leading to inhibition of the growth of a cancer cell. Thus, both Song and You references taken individually or combined fail to provide an agent that inhibits Dvl-3 expression as required by Applicants' Claims 31 and 36. Therefore, both Song and You fail to provide all elements and limitations of Applicants' claims.

As the combination of references suggested in the Office Action *fails to provide all of the elements* of Applicants' claimed invention, a *prima facie* case of obviousness has not been set forth. Therefore, Applicants respectfully request the rejection of Claims 31 and 36 under 35 U.S.C § 103(a) be withdrawn.

2. ***There Is No Motivation To Make The Suggested Combination And No Reasonable Expectation Of Success***

As discussed *supra*, there is nothing in the Song and You references that teach a method for inhibiting the growth of a cancer cell with an agent for inhibiting Dvl-3 expression and achieving inhibition of the growth of the cancer cell. Therefore, one of ordinary skill in the art would not be motivated to combine the teaching of Song and You to arrive at Applicants' invention.

As the references suggested in the Office Action *fail to motivate to make the suggested combination* of Applicants' claimed invention and *fail to provide a reasonable expectation of success*, Applicants' invention cannot be obvious in view of the cited art. A *prima facie* case of obviousness has not been set forth. Therefore, Applicants respectfully request the rejection of Claims 31 and 36 under 35 U.S.C § 103(a) be withdrawn.

3. ***Without The Benefit Of Impermissible Hindsight, The Claimed Invention Was Not Obvious At The Time It Was Invented***

In *KSR*, the Court also cautioned against the use of impermissible hindsight. *KSR* at 1742. ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning."). Applicants respectfully submit that, without the teachings of the instant specification, one of skill in the art would not have known at the time the invention was made to inhibit the growth of a cancer cell overexpressing a

Dvl-3 protein with an agent that inhibits Dvl-3 expression. The presently claimed method provides a new way of inhibiting the growth of a cancer cell that is not suggested by the Song and/or You references. Identifying the claimed invention in a publication ("Uematsu") which was published in the journal *Oncogene* on October 16, 2003 by the inventive group of the instant application (Applicants He, You, Xu, and Jablons) after the filing date of the instant application and after its effective filing date, to allegedly fit the elements of the claims requires hindsight provided by the claimed invention. This, as emphasized in both the case law and the MPEP, is impermissible. Further, as declared in the accompanying 131 Declaration, Kazutsugu Uematsu, the first author of "Uematsu" was a post-doctoral fellow in Applicants' laboratory who worked under the supervision of Applicants.

Therefore, Applicants respectfully request the rejection of Claims 31 and 36 under 35 U.S.C § 103(a) be withdrawn.

E. ***Rejection of Claims 31 and 36 Over Alsobrook And You As Evidenced by Uematsu***

The Examiner rejected Claims 31 and 36 under 35 U.S.C. § 103(a) as being unpatentable over Alsobrook in view of You as evidenced by Uematsu. According to the Examiner, a method of inhibiting a mesothelioma cell with an agent that effects Dvl-3 expression was *prima facie* obvious at the time of the invention over Alsobrook in view of You. The Examiner acknowledged that Alsobrook does not teach using the method of inhibiting cancer cell growth in a mesothelioma and cites to You to provide this teaching.

The rejection is respectfully traversed.

As an initial matter, in view of the rule 131 Declaration, Alsobrook does not qualify as prior art under 35 U.S.C. § 102(e). On this basis alone, this rejection under 35 U.S.C. 103(a) should be withdrawn.

The shortcomings of the teachings of You, Alsobrook's '928 Application, and Alsobrook's provisional patent applications have been discussed *supra*. In view of the arguments provided herein *supra* and because Alsobrook does not qualify as prior art under § 102(e), this

rejection should be withdrawn. Reciting to Uematsu, as discussed, *supra*, constitutes impermissible hindsight.

As such, the Examiner did not present a *prima facie* case of obviousness. Applicants respectfully request the rejection of Claims 31 and 36 under 35 U.S.C § 103(a) as being unpatentable over Alsobrook in view of You as evidenced by Uematsu be withdrawn.

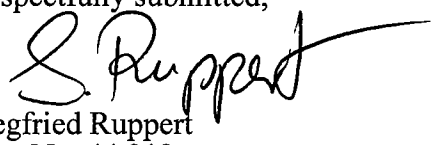
CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no fee is required. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from or credit any overpayment to, the above-noted Deposit Account.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 415-576-0200.

Respectfully submitted,



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Attachments (Exhibit A; Rule 1.131 Declaration, including Exhibits 1-11)
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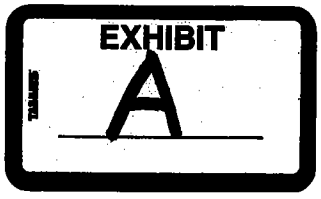
PROVISIONAL PATENT APPLICATION

In the name of the inventor

Weizhen Ji

832C. Novel Splice Variant of Dishevelled-3-like Proteins and Nucleic Acids Encoding Same



Novel Splice Variant of Dishevelled-3-like Proteins and Nucleic Acids Encoding Same

The present invention discloses a novel protein encoded by a cDNA and/or by genomic DNA and proteins similar to it, namely, new proteins bearing sequence similarity to Dishevelled-3, nucleic acids that encode these proteins or fragments thereof, and antibodies that bind immunospecifically to a protein of the invention.

Background

The Drosophila dishevelled gene (dsh) encodes a cytoplasmic phosphoprotein (Klingensmith et al., 1994) that regulates cell proliferation, acting as a transducer molecule for developmental processes, including segmentation and neuroblast specification. Pizzuti et al. (1996) noted that dsh is required for the function of the wingless gene product wg, a segment polarity gene homologous to the mammalian protooncogene WNT1 (164820). The Dishevelled specific domain, specific to the signaling protein disheveled, is found adjacent to the PDZ domain (IPR001478), often in conjunction with DEP (IPR000591) and DIX (IPR001158). Pizzuti et al. (1996) reported the isolation and chromosomal mapping of 2 human dsh homologs, designated DVL1 and DVL3 by them. The human dsh homologs were isolated from a fetal brain cDNA library. DVL3 encodes a predicted 716-amino acid polypeptide that shows 74% nucleotide homology with human DVL1 and 71% homology with the mouse Dvl1 gene. DVL1 and DVL3 share 64% amino acid identity. Pizzuti et al. (1996) reported that homology is particularly high in the N-terminal region and that there is more divergence in the C-terminal regions. PCR carried out using DNA from rodent human somatic cell hybrids and DVL3 specific primers led to the assignment of DVL3 to human chromosome 3. Pizzuti et al. (1996) regionally assigned DVL3 to band 3q27 using fluorescence in situ hybridization. Hybridization of poly(A) mRNA with the DVL3 cDNA revealed a 2.9-kb transcript with abundant expression in skeletal muscle, pancreas and heart. They also detected 5.9-kb and 5.0-kb transcripts in skeletal muscle, adult liver, adult heart, pancreas, and placenta. The 5.9-kb form was abundant in fetal tissues but the 5.0-kb form was absent from these tissues. Pizzuti et al. (1996) noted that Charcot-Marie-Tooth type 2B maps to chromosome 3q.

Bui et al. (1997) also isolated human DVL3, which shares 98% amino acid identity with mouse Dvl3 and 49% with Drosophila dsh. The authors confirmed the chromosomal localization at 3p27. Semenov and Snyder (1997) isolated 3 human genes encoding proteins homologous to Drosophila dsh. The cDNA sequence of DVL3 reported by Semenov and Snyder (1997) differs from the previously reported sequences deposited in GenBank. Bui et al. (1997) detected expression of DVL3 mRNA in B cells, breast, kidney, bladder, endometrium, and 2 primary endometrial cultures. It was detected equally in normal human breast tissues and tumors and in colorectal samples of normal tissues, polyps, and tumors.

The sequence disclosed in the application represents a splice variant of human dishevelled 3 (DVL3), lacking a 363 bp long coding region containing a PDZ domain.

References

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2. Klingensmith, J.; Nusse, R.; Perrimon, N. : The Drosophila segment polarity gene dishevelled encodes a novel protein required for response to wingless signal. Genes Dev. 8: 118-130, 1994. PubMed ID : 8288125

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4. Semenov, M. V.; Snyder, M. : Human dishevelled genes constitute a DHR-containing multigene family. Genomics 42: 302-310, 1997. PubMed ID : 9192851

Brief Description of the Drawings

Figure 1. Nucleotide sequence encoding the Dishevelled-3-like protein (Acc. No. CG164330-01) of the invention.

Figure 2. Protein sequence encoded by the nucleotide sequence shown in Figure 1.

Figure 3A. A high-scoring match as determined by a BLASTN search of GenBank Composite (no HTG) dated 12/21/01 using the sequence of the Dishevelled-3-like gene of the invention.

Figure 3B. A high-scoring match as determined by a BLASTP search (versus Non-Redundant Composite dated 12/21/01) using the sequence of the Dishevelled-3-like protein of the invention.

Figure 3C. BLASTN identity search of CuraGen Corporation's human SeqCalling database using the Dishevelled-3-like gene of the invention.

Figure 4. ClustalW alignment of the protein of Acc. No. CG164330-01 with similar Dishevelled-3s.

Figure 5: PSORT, SignalP and hydropathy results for the Dishevelled-3-like protein of Acc. No. CG164330-01.

Description of the Invention

Method of Identifying the Nucleic Acid Encoding the Dishevelled-3-Like Protein.

The sequence of Acc. No. CG164330-01 was derived by laboratory cloning of cDNA fragments, by *in silico* prediction of the sequence. cDNA fragments covering either the full length of the DNA sequence, or part of the sequence, or both, were cloned. *In silico* prediction was based on

sequences available in Curagen's proprietary sequence databases or in the public human sequence databases, and provided either the full length DNA sequence, or some portion thereof.

The laboratory cloning was performed using one or more of the methods summarized below:

SeqCalling™Technology: cDNA was derived from various human samples representing multiple tissue types, normal and diseased states, physiological states, and developmental states from different donors. Samples were obtained as whole tissue, primary cells or tissue cultured primary cells or cell lines. Cells and cell lines may have been treated with biological or chemical agents that regulate gene expression, for example, growth factors, chemokines or steroids. The cDNA thus derived was then sequenced using CuraGen's proprietary SeqCalling technology. Sequence traces were evaluated manually and edited for corrections if appropriate. cDNA sequences from all samples were assembled together, sometimes including public human sequences, using bioinformatic programs to produce a consensus sequence for each assembly. Each assembly is included in CuraGen Corporation's database. Sequences were included as components for assembly when the extent of identity with another component was at least 95% over 50 bp. Each assembly represents a gene or portion thereof and includes information on variants, such as splice forms single nucleotide polymorphisms (SNPs), insertions, deletions and other sequence variations.

Variant sequences are also included in this application. A variant sequence can include a single nucleotide polymorphism (SNP). A SNP can, in some instances, be referred to as a "cSNP" to denote that the nucleotide sequence containing the SNP originates as a cDNA. A SNP can arise in several ways. For example, a SNP may be due to a substitution of one nucleotide for another at the polymorphic site. Such a substitution can be either a transition or a transversion. A SNP can also arise from a deletion of a nucleotide or an insertion of a nucleotide, relative to a reference allele. In this case, the polymorphic site is a site at which one allele bears a gap with respect to a particular nucleotide in another allele. SNPs occurring within genes may result in an alteration of the amino acid encoded by the gene at the position of the SNP. Intragenic SNPs may also be silent, when a codon including a SNP encodes the same amino acid as a result of the redundancy of the genetic code. SNPs occurring outside the region of a gene, or in an intron within a gene, do not result in changes in any amino acid sequence of a protein but may result in altered regulation of the expression pattern. Examples include alteration in temporal expression, physiological response regulation, cell type expression regulation, intensity of expression, and stability of transcribed message.

One or more genomic clones AC048331, AC061705, AC092931 on chromosome 3 were identified by TBLASTN using CuraGen Corporation's sequence file for members of Dishevelled-3 and/or the Dishevelled family, run against the genomic daily files made available by GenBank or obtained from Human Genome Project Sequencing centers. These sequences were analyzed for putative coding regions as well as for similarity to known DNA and protein sequences. Programs used for these analyses include Grail, Genscan, BLAST, HMMER, FASTA, Hybrid and other relevant programs. Putative coding regions were spliced from the genomic clone and then concatenated using a known homolog for reference. The derived sequence may have been further extended using additional genomic clones showing greater than 98% identity to the open reading frame.

The regions defined by the procedures described above were then manually integrated and corrected for apparent inconsistencies that may have arisen, for example, from miscalled bases in the original fragments or from discrepancies between predicted exon junctions, and regions of sequence similarity, to derive the final sequence disclosed herein. When necessary, the process to identify and analyze genomic clones was reiterated to derive the full length sequence. The following public components were thus included in the invention: AC048331, AC061705, AC092931.

The DNA sequence was analyzed to identify any open reading frames encoding novel full length proteins as well as novel splice forms of these genes. The DNA sequence and protein sequence for a novel Dishevelled-3-like gene are reported here as CuraGen Acc. No. CG164330-01.

Results

The novel nucleic acid of 2634 nucleotides (designated CuraGen Acc. No. CG164330-01) encoding a novel Dishevelled-3-like protein is shown in Fig. 1. An open reading frame was identified beginning at nucleotides 51-53 and ending at nucleotides 1836-1838. This open reading from begins with an ATG initiation codon and ends with a TGA stop codon. This polypeptide represents a novel functional Dishevelled-3-like protein. The start and stop codons of the open reading frame are highlighted in bold type. Putative untranslated regions (underlined), if any, are found upstream from the initiation codon and downstream from the termination codon. The encoded protein having 595 amino acid residues is presented using the one-letter code in Fig. 2.

Similarities

In a search of sequence databases, it was found, for example, that the nucleic acid sequence of this invention has 1325 of 1501 bases (88%) identical to a gb:GENBANK-ID:AF006013|acc:AF006013.1 mRNA from Homo sapiens (Homo sapiens dishevelled 3 (DVL3) mRNA, complete cds) (Fig. 3A). The full amino acid sequence of the protein of the invention was found to have 336 of 336 amino acid residues (100%) identical to, and 336 of 336 amino acid residues (100%) similar to, the 716 amino acid residue ptnr:SWISSPROT-ACC:Q92997 protein from Homo sapiens (Human) (Segment polarity protein dishevelled homolog DVL-3 (Dishevelled-3) (DSH homolog 3))(Fig. 3B).

A multiple sequence alignment is given in Fig. 4, with the protein of the invention being shown on the first line in a ClustalW analysis comparing the protein of the invention with related protein sequences. Please note this sequence represents a splice form of Dishevelled-3 as indicated in positions 260 to 381 aa.

The presence of identifiable domains in the protein disclosed herein was determined by searches versus domain databases such as Pfam, PROSITE, ProDom, Blocks or Prints and then identified by the Interpro domain accession number. Significant domains are summarized in Table 1.

Scores for sequence family classification (score includes all domains):

Model	Description	Score	E-value	N
DIX (InterPro)	DIX domain	194.5	1.7e-54	1
Dishevelled (InterPro)	Dishevelled specific domain	136.6	4.5e-37	1
DEP (InterPro)	Domain found in Dishevelled, Egl-10, and	121.1	2e-32	1
oxidored_q1 (InterPro)	NADH-Ubiquinone/plastoquinone (complex I)	3.5	5.1	1

Parsed for domains:

Model	Domain	seq-f	seq-t		hmm-f	hmm-t		score	E-value
DIX	1/1	1	82	[.	1	86	[]	194.5	1.7e-54
Dishevelled	1/1	142	213	..	1	74	[]	136.6	4.5e-37
oxidored_q1	1/1	245	272	..	291	316	.]	3.5	5.1
DEP	1/1	301	375	..	1	89	[]	121.1	2e-32

describe domains and functional relevance

Dishevelled (Dsh) protein is an important component of the Wnt signal-transduction pathway. It has three relatively conserved domains: DIX, PDZ and DEP. The DIX domain of Dvl-1 (a mammalian Dishevelled homolog) shares 37% identity with the C-terminal region of Axin. Dsh can interact with the Axin/APC/GSK3/beta-catenin complex, and may thus modulate its activity.

The Wnt signaling pathway is conserved in various species from worms to mammals, and plays important roles in development, cellular proliferation, and differentiation. The molecular mechanisms by which the Wnt signal regulates cellular functions are becoming increasingly well understood. Wnt stabilizes cytoplasmic beta-catenin, which stimulates the expression of genes including c-myc, c-jun, fra-1, and cyclin D1. Axin and its homolog Axil are components of the Wnt signaling pathway that negatively regulate this pathway. Other components of the Wnt signaling pathway, including Dvl, glycogen synthase kinase-3beta (GSK-3beta), beta-catenin, and adenomatous polyposis coli (APC), interact with Axin, and the phosphorylation and stability of beta-catenin are regulated in the Axin complex. Axil has similar functions to Axin. Thus, Axin and Axil act as scaffold proteins in the Wnt signaling pathway, thereby modulating the Wnt-dependent cellular functions.

The Dishevelled specific domain is specific to the signaling protein dishevelled. In Drosophila, the dishevelled segment polarity protein is required to establish coherent arrays of polarized cells and segments in embryos. It plays a role in wingless signaling, possibly through the reception of the wingless signal by target cells and subsequent redistribution of arm protein in response to that signal in embryos. The domain is found adjacent to the PDZ domain (IPR001478), often in conjunction with DEP (IPR000591) and DIX (IPR001158).

This indicates that the sequence of the invention has properties similar to those of other proteins known to contain this/these domain(s) and similar to the properties of these domains.

Chromosomal information:

The Dishevelled-3-like gene disclosed in this invention maps to chromosome 3. This assignment was made using mapping information associated with genomic clones, public genes and ESTs sharing sequence identity with the disclosed sequence and CuraGen Corporation's Electronic Northern bioinformatic tool.

Tissue expression

The Dishevelled-3-like gene disclosed in this invention is expressed in at least the following tissues: fetal brain, fetal liver/spleen, melanocyte, placenta, ovary (tumor), breast, fetal heart, colon, uterus (pregnant), brain-hippocampus, embryo, parathyroid gland (tumor), heart, fetal lung. Expression information was derived from the tissue sources of the sequences that were included in the derivation of the sequence of CuraGen Acc. No. CG164330-01.

Cellular Localization and Sorting

The PSORT, SignalP and hydropathy profile for the Dishevelled-3-like protein are shown in Fig. 5. The results predict that this sequence has no signal peptide and is likely to be localized in the nucleus with a certainty of 0.7000 predicted by PSORT. The hydropathy profile is characteristic of this gene family.

Functional Variants and Homologs

The novel nucleic acid of the invention encoding a Dishevelled-3-like protein includes the nucleic acid whose sequence is provided in Fig. 1, or a fragment thereof. The invention also includes a mutant or variant nucleic acid any of whose bases may be changed from the corresponding base shown in Fig. 1 while still encoding a protein that maintains its Dishevelled-3-like activities and physiological functions, or a fragment of such a nucleic acid. The invention further includes nucleic acids whose sequences are complementary to the sequence of CuraGen Acc. No. CG164330-01, including nucleic acid fragments that are complementary to any of the nucleic acids just described. The invention additionally includes nucleic acids or nucleic acid fragments, or complements thereto, whose structures include chemical modifications. Such modifications include, by way of non-limiting example, modified bases, and nucleic acids whose sugar phosphate backbones are modified or derivatized. These modifications are carried out at least in part to enhance the chemical stability of the modified nucleic acid, such that they may be used, for example, as antisense binding nucleic acids in therapeutic applications in a subject. In the mutant or variant nucleic acids, and their complements, up to about 12% of the bases may be so changed.

The novel protein of the invention includes the Dishevelled-3-like protein whose sequence is provided in Fig. 2. The invention also includes a mutant or variant protein any of whose residues may be changed from the corresponding residue shown in Fig. 2 while still encoding a protein that maintains its Dishevelled-3-like activities and physiological functions, or a functional

fragment thereof. In the mutant or variant protein, up to about 0% of the amino acid residues may be so changed.

Chimeric and Fusion Proteins

The present invention includes chimeric or fusion proteins of the Dishevelled-3-like protein, in which the Dishevelled-3-like protein of the present invention is joined to a second polypeptide or protein that is not substantially homologous to the present novel protein. The second polypeptide can be fused to either the amino-terminus or carboxyl-terminus of the present CG164330-01 polypeptide. In certain embodiments a third nonhomologous polypeptide or protein may also be fused to the novel Dishevelled-3-like protein such that the second nonhomologous polypeptide or protein is joined at the amino terminus, and the third nonhomologous polypeptide or protein is joined at the carboxyl terminus, of the CG164330-01 polypeptide. Examples of nonhomologous sequences that may be incorporated as either a second or third polypeptide or protein include glutathione S-transferase, a heterologous signal sequence fused at the amino terminus of the Dishevelled-3-like protein, an immunoglobulin sequence or domain, a serum protein or domain thereof (such as a serum albumin), an antigenic epitope, and a specificity motif such as $(His)_6$.

The invention further includes nucleic acids encoding any of the chimeric or fusion proteins described in the preceding paragraph.

Antibodies

The invention further encompasses antibodies and antibody fragments, such as Fab, $(Fab)_2$ or single chain FV constructs, that bind immunospecifically to any of the proteins of the invention. Also encompassed within the invention are peptides and polypeptides comprising sequences having high binding affinity for any of the proteins of the invention, including such peptides and polypeptides that are fused to any carrier particle (or biologically expressed on the surface of a carrier) such as a bacteriophage particle.

Uses of the Compositions of the Invention

The protein similarity information, expression pattern, cellular localization, and map location for the protein and nucleic acid disclosed herein suggest that this Dishevelled-3-like protein may have important structural and/or physiological functions characteristic of the Dishevelled family. Therefore, the nucleic acids and proteins of the invention are useful in potential diagnostic and therapeutic applications and as a research tool. These include serving as a specific or selective nucleic acid or protein diagnostic and/or prognostic marker, wherein the presence or amount of the nucleic acid or the protein are to be assessed. These also include potential therapeutic applications such as the following: (i) a protein therapeutic, (ii) a small molecule drug target, (iii) an antibody target (therapeutic, diagnostic, drug targeting/cytotoxic antibody), (iv) a nucleic acid useful in gene therapy (gene delivery/gene ablation), (v) an agent promoting tissue regeneration *in vitro* and *in vivo*, and (vi) a biological defense weapon.

The nucleic acids and proteins of the invention have applications in the diagnosis and/or treatment of various diseases and disorders. For example, the compositions of the present

invention will have efficacy for the treatment of patients suffering from: adrenoleukodystrophy, Alzheimer's disease, autoimmune disease, allergies, addiction, anxiety, ataxia-telangiectasia, asthma, ARDS, atherosclerosis, behavioral disorders, aortic stenosis, atrial septal defect (ASD), atrioventricular (A-V) canal defect, ductus arteriosus, allergy, cerebral palsy, congenital adrenal hyperplasia, cirrhosis, cardiomyopathy, congenital heart defects, diabetes, diverticular disease, epilepsy, emphysema, endometriosis, endocrine dysfunctions, graft versus host disease, glomerulonephritis, graft versus host disease (GVHD), growth and reproductive disorders, hemophilia, hypercoagulation, hypercalceimia, Huntington's disease, hypertension, hypogonadism, fertility, idiopathic thrombocytopenic purpura, immunodeficiencies, interstitial nephritis, IgA nephropathy, lymphaedema, inflammatory bowel disease, Lesch-Nyhan syndrome, leukodystrophies, multiple sclerosis, muscular dystrophy, myasthenia gravis, neurodegeneration, neuroprotection,obesity, Parkinson's disease, pain, polycystic kidney disease, pulmonary stenosis, pancreatitis, renal artery stenosis, renal tubular acidosis, stroke, systemic lupus erythematosus, scleroderma, subaortic stenosis, transplantation, tuberous sclerosis, Von Hippel-Lindau (VHL) syndrome, ventricular septal defect (VSD), valve diseases, Von Hippel-Lindau (VHL) syndrome, ulcers, cancers as well as other diseases, disorders and conditions.

These materials are further useful in the generation of antibodies that bind immunospecifically to the novel substances of the invention for use in diagnostic and/or therapeutic methods.

FIGURES

Figure 1. Nucleotide sequence encoding the Dishevelled-3-like protein of the invention.

>CG164330_01

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CGGCCGCCCGAGCAGGCCGCGCGCGGGCCGCCGGGCCCGAGGCCAGAGCCATGGGCGAGA      60
CCAAGATCATCTACCACTTGGATGGGCAGGAGACGCCGTACCTTGTGAAGCTGCCCCTGC     120
CCGCCGAGCGCGTCACCTTGGCGGACTTTAAGGGCGTTTTGCAGCGACCCAGCTATAAGT     180
TCTTCTTCAAGTCTATGGACGACGATTTCGGAGTGGTGAAGGAGGAGATCTCGGATGACA     240
ATGCCAAGCTACCATGCTTCAATGGCCGGGTGGTGTCCTGGCTGGTGTCAGCTGAGGGCT     300
CACACCCAGACCCAGCCCCCTTCTGTGCTGATAACCCATCGGAGCTGCCACCACCTATGG     360
AGCGCACGGGAGGCATCGGGGACTCCCGACCCCCATCCTTCCACCCTCATGCTGGTGGGG     420
GCAGCCAGGAGAACCTGGACAATGACACAGAGACGGACTCTTTGGTGTCTGCCCAGCGAG     480
GGCGGCCACGCCGGAGGGATGGCCCAGAGCATGCAACCCGGCTAAATGGAACTGCGAAGG     540
GGGAACGGCGGCGAGGACCAGGGGGTTATGATAGCTCATCCACCCTTATGAGCAGTGAGC     600
TGGAGACCACCAGCTTCTTTGACTCAGATGAGGATGACTCCACCAGCAGGTTCAGCAGCT     660
CCACAGAACAGAGCAGTGCCTCACGCCTGATGAGAAGACACAAGCGGCGGCGGCGGAAGC     720
AGAAGGTTTCTCGGATTGAGCGGTCCTCGTCCTTCAGCAGCATCACGGACTCCACCATGT     780
CACTCAACATCATCACGGTCACTCTCAACATGGAAAAATATAACTTCTTGAGCACCATCA     840
CCTCCACCAGCTCCTCCATCACCAGTTCCATCCCTGACACAGAGCGCCTAGACGACTTCC     900
ACTTGTCCATCCACAGTGACATGGCTGCCATCGTAAAAGCCATGGCCTCCCCTGAATCAG     960
GGTTGGAGGTCCGTGACCGCATGTGGCTCAAGATTACCATCCCTAATGCTTTCATCGGCT    1020
CAGATGTGGTGGACTGGCTGTACCACAATGTGGAAGGCTTCACGGACCGGAGGGAGGCCC    1080
GCAAGTATGCCAGCAACCTGCTGAAAGCTGGCTTCATCCGCCATACCGTCAACAAGATCA    1140
CCTTCTCCGAGCAGTGCTACTACATCTTCGGTGACCTCTGCGGCAACATGGCCAACCTGT    1200
CTCTCCACGATCACGATGGCTCCAGTGGCGCCTCTGACCAGGACACACTGGCCCCTTTGC    1260
CGCACCCGGGGGCCGCCCCTTGGCCCATGGCTTTCCCGTACCAGTACCCGCCACCCCCGC    1320
ACCCATACAACCCGCACCCGGGCTTCCCGGAGCTGGGCTACAGCTACGGCGGGGGCAGCG    1380
CCAGCAGTCAGCACAGCGAAGGCAGTCGGAGCAGTGGCTCCAACCGTAGCGGCAGCGATC    1440
GGAGGAAGGAGAAGGACCCGAAGGCCGGGGACTCCAAGTCCGGGGGCAGCGGCAGCGAAT    1500
CGGACCACACCACACGCAGCAGCCTGCGGGGGCCGCGGGAGCGGGCGCCCAGCGAGCGCT    1560
CAGGGCCGGCGGCCAGCGAGCACAGCCACCGCAGCCACCATTCCCTGGCCAGCAGCCTTC    1620
GCAGCCACCACACACACCCGAGCTACGGTCCTCCCGGAGTGCCCCCTCTCTACGGCCCCC    1680
CCATGCTGATGATGCCCCCGCCGCCCGCGGCCATGGGGCCCCCAGGAGCCCCTCCGGGCC    1740
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GCGACCTGGCCTCAGTGCCCCCGGAACTGACCGCCAGCAGACAGTCCTTCCGCATGGCCA   1800
TGGGAAACCCCAGTGAGTTCTTTGTGGATGTGATGTGAGCAGGGCCCCTCCCCCAGCTCC   1860
ATTCCGCTCCCACCCCAGCCGGCTGCGTTCCTCTCTCCATCCGTCCGTCTTTTTTACTTT   1920
GTCTGGTACCTGAAAGGGAAATAAAAGGAACTAAATCCAGGTGCGCTAACTGCTCGCAGG   1980
GTGCTGCGAGGGTGGGGTGCACCTACCGATTGGCTCTGCAGCCCCCTAACCTGCCTCTGG   2040
CCCCAGTTCGTTTCCTCTGCCCACTAATCCCTGCGCAGGACTTCCCAGGACCCCTTTTGT   2100
CTCTGGGACCAGACTTGTTGGTGCTACCCCTTACTCCCCTCTGCAACCCCCATTTTGGGA   2160
GTTGACCCCAGCAATGACCTTGGTGGCACGCTCACTCCCTCATTCTCTCGTTTCCCCTTT   2220
AGCTCCCTTTCACCATTTATTCAGCTACATCATCCCTCTATTAACCCCACCCCATCAGGC   2280
ACGTGTGCAAACCTCTTGACTTTACCCCACATTACTGAAACCAAAATATATTTGCTTCAT   2340
CTGCCCCTACTAACCATCCCCCTGCCTGCTGCCTCAGTCCTGCAACCTAAAGCTGTAGTC   2400
GCCTCCAATAGCCATCCATGCCATCCCTGCCTGTGCCTAGATCAGAGGCCCAGAGGGCCC   2460
CCTCAGTTGCCTGAGCAGCTGGTGGCTTCCAGGGAGCATCTCTGCTCTACCCCTGCCCCA   2520
TGCCTGCCCTGCGTGCTGGTTCCTTCAGACCCCTAACCCTACTAACCAGCAGGCTCATCT   2580
CACCTCCAGGCCTGAAACATTTCTTTTCTTTCTTTTTTCCTCCCCCAATTTACC   2634
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Figure 2. Protein sequence encoded by the nucleotide sequence shown in Figure 1.

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>CG164330_01
MGETKIIYHLDGQETPYLVKLPLPAERVTLADFKGVLQRPSYKFFFKSMDDDFGVVKEEI    60
SDDNAKLPCFNGRVVSWLVSAEGSHPDPAPFCADNPSELPPPMERTGGIGDSRPPSFHPH   120
AGGGSQENLDNDTETDSLVSAQRGRPRRRDGPEHATRLNGTAKGERRRGPGGYDSSSTLM   180
SSELETTSFFDSDEDDSTSRFSSSTEQSSASRLMRRHKRRRRKQKVSRIERSSSFSSITD   240
STMSLNIITVTLNMEKYNFLSTITSTSSSITSSIPDTERLDDFHLSIHSDMAAIVKAMAS   300
PESGLEVRDRMWLKITIPNAFIGSDVVDWLYHNVEGFTDRREARKYASNLLKAGFIRHTV   360
NKITFSEQCYYIFGDLCGNMANLSLHDHDGSSGASDQDTLAPLPHPGAAPWPMAFPYQYP   420
PPPHPYNPHPGFPELGYSYGGGSASSQHSEGSRSSGSNRSGSDRRKEKDPKAGDSKSGGS   480
GSESDHTTRSSLRGPRERAPSERSGPAASEHSHRSHHSLASSLRSHHTHPSYGPPGVPPL   540
YGPPMLMMPPPPAAMGPPGAPPGRDLASVPPELTASRQSFRMAMGNPSEFFVDVM    595
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Figure 3A. BLASTN search using CuraGen Acc. No. CG164330-01.

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>gb:GENBANK-ID:AF006013|acc:AF006013.1 Homo sapiens dishevelled 3 (DVL3) mRNA,
            complete cds - Homo sapiens, 2286 bp.
            Length = 2286

  Plus Strand HSPs:

 Score = 5641 (846.4 bits), Expect = 4.8e-249, P = 4.8e-249
 Identities = 1325/1501 (88%), Positives = 1325/1501 (88%), Strand = Plus /
Plus

Query:   459 TCTTTGGTGTCTGCCCAGCGAGGGCGGCCACGCCG-GAGGGATGGCCCAGAGCATGCAAC 517
             TCTT GG  TCT CC A  G GGGC     C  CG G G G TG C   G GCAT C AC
Sbjct:   787 TCTTGGGCATCT-CC-ATTGTGGGCCAAAGCAACGAGCGTGGTGACGGCG-GCAT-CTAC 842

Query:   518 CC-GGCTAAATGGAACTGCGAAGGGGGAACGGCGGC-GA-GGAC-CAGGGGGTTATGA-- 571
                GGCT  AT      G G  GGGG    GGC GC GA GGAC CA  G G  A GA
Sbjct:   843 ATTGGCTCTATCATGAAGGGT-GGGGCCGTGGCTGCTGATGGACGCATCGAGCCAGGAGA 901

Query:   572 TA-GCTCATCCACCCTTATGAGCAGTGAGCTG-GAGACCACCAGCTTCTTT-GACTCAGA 628
             TA G T  T CA     A GAG A T A CT  GAGA CA  AG T  T   GA  CAG
Sbjct:   902 TATGTTGTTACAGGTAAACGAG-A-TCAACTTTGAGAACATGAG-TAATGACGATGCAG- 957

Query:   629 TGAGGATGACTCCACCAGCAGGTTCAGCAGCTCCACAGAACAGAGCAGTGCCTCACGCCT 688
             T  GG T ACT C   AG   GT CA CA   CC   G  CA   C  TG CT   GCC
Sbjct:   958 TCCGGGT-ACTGCGGGAGATTGTGCA-CAAA-CCGGGGCCCATCACCCTGACTGTAGCCA 1014
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Query:   689 GATGAGAAGACACAAGCGGCGGCGGCGGAAGCAGAAGGTTTCTC-GGATTGAGCGG-TCC 746
               TG    GAC CAAG   C  CG  GG  GC   A  TT C C GGA  GAGC   TCC
Sbjct:  1015 AGTGCTGGGACCCAAGTC-CA-CGT-GGTTGCTTCACATTGCCCAGGAGCGAGCCCATCC 1071

Query:   747 TCGTCC-TTCAGCA-GCATCACGGA-CTCCACCA-TGTCACTCAACATCATCACGGTCAC 802
               G CC TT A C  GC  C  GG  CTCC  CA TG CA  CA  A C  CAC  TC C
Sbjct:  1072 G-GCCCATTGACCCTGCGGCCTGGGTCTCCCACACTG-CAGCCATGACCGGCACCTTCCC 1129

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               T  CA  A GG A  A     CT C TGAGCACCATCACCTCCACCAGCTCCTCCATCAC
Sbjct:  1130 TG-CAT-ACGGCATGAGCCC-CTCCCTGAGCACCATCACCTCCACCAGCTCCTCCATCAC 1186

Query:   863 CAGTTCCATCCCTGACACAGAGCGCCTAGACGACTTCCACTTGTCCATCCACAGTGACAT 922
               CAGTTCCATCCCTGACACAGAGCGCCTAGACGACTTCCACTTGTCCATCCACAGTGACAT
Sbjct:  1187 CAGTTCCATCCCTGACACAGAGCGCCTAGACGACTTCCACTTGTCCATCCACAGTGACAT 1246

Query:   923 GGCTGCCATCGTAAAAGCCATGGCCTCCCCTGAATCAGGGTTGGAGGTCCGTGACCGCAT 982
               GGCTGCCATCGTAAAAGCCATGGCCTCCCCTGAATCAGGGTTGGAGGTCCGTGACCGCAT
Sbjct:  1247 GGCTGCCATCGTAAAAGCCATGGCCTCCCCTGAATCAGGGTTGGAGGTCCGTGACCGCAT 1306

Query:   983 GTGGCTCAAGATTACCATCCCTAATGCTTTCATCGGCTCAGATGTGGTGGACTGGCTGTA 1042
               GTGGCTCAAGATTACCATCCCTAATGCTTTCATCGGCTCAGATGTGGTGGACTGGCTGTA
Sbjct:  1307 GTGGCTCAAGATTACCATCCCTAATGCTTTCATCGGCTCAGATGTGGTGGACTGGCTGTA 1366

Query:  1043 CCACAATGTGGAAGGCTTCACGGACCGGAGGGAGGCCCGCAAGTATGCCAGCAACCTGCT 1102
               CCACAATGTGGAAGGCTTCACGGACCGGAGGGAGGCCCGCAAGTATGCCAGCAACCTGCT
Sbjct:  1367 CCACAATGTGGAAGGCTTCACGGACCGGAGGGAGGCCCGCAAGTATGCCAGCAACCTGCT 1426

Query:  1103 GAAAGCTGGCTTCATCCGCCATACCGTCAACAAGATCACCTTCTCCGAGCAGTGCTACTA 1162
               GAAAGCTGGCTTCATCCGCCATACCGTCAACAAGATCACCTTCTCCGAGCAGTGCTACTA
Sbjct:  1427 GAAAGCTGGCTTCATCCGCCATACCGTCAACAAGATCACCTTCTCCGAGCAGTGCTACTA 1486

Query:  1163 CATCTTCGGTGACCTCTGCGGCAACATGGCCAACCTGTCTCTCCACGATCACGATGGCTC 1222
               CATCTTCGGTGACCTCTGCGGCAACATGGCCAACCTGTCTCTCCACGATCACGATGGCTC
Sbjct:  1487 CATCTTCGGTGACCTCTGCGGCAACATGGCCAACCTGTCTCTCCACGATCACGATGGCTC 1546

Query:  1223 CAGTGGCGCCTCTGACCAGGACACACTGGCCCCTTTGCCGCACCCGGGGGCCGCCCCTTG 1282
               CAGTGGCGCCTCTGACCAGGACACACTGGCCCCTTTGCCGCACCCGGGGGCCGCCCCTTG
Sbjct:  1547 CAGTGGCGCCTCTGACCAGGACACACTGGCCCCTTTGCCGCACCCGGGGGCCGCCCCTTG 1606

Query:  1283 GCCCATGGCTTTCCCGTACCAGTACCCGCCACCCCCGCACCCATACAACCCGCACCCGGG 1342
               GCCCATGGCTTTCCCGTACCAGTACCCGCCAC CCCGCACCCATACAACCCGCACCCGGG
Sbjct:  1607 GCCCATGGCTTTCCCGTACCAGTACCCGCCACGCCCGCACCCATACAACCCGCACCCGGG 1666

Query:  1343 CTTCCCGGAGCTGGGCTACAGCTACGGCGGGGGCAGCGCCAGCAGTCAGCACAGCGAAGG 1402
               CTT   GGAGCTGGGCTACAGCTACGGCGGGGGCAGCGCCAGCAGTCAGCACAGCGAAGG
Sbjct:  1667 CTTGGGGGAGCTGGGCTACAGCTACGGCGGGGGCAGCGCCAGCAGTCAGCACAGCGAAGG 1726

Query:  1403 CAGTCGGAGCAGTGGCTCCAACCGTAGCGGCAGCGATCGGAGGAAGGAGAAGGACCCGAA 1462
               CAGTCGGAGCAGTGGCTCCAACCGTAGCGGCAGCGATCGGAGGAAGGAGAAGGACCCGAA
Sbjct:  1727 CAGTCGGAGCAGTGGCTCCAACCGTAGCGGCAGCGATCGGAGGAAGGAGAAGGACCCGAA 1786

Query:  1463 GGCCGGGGACTCCAAGTCCGGGGGCAGCGGCAGCGAATCGGACCACACCACACGCAGCAG 1522
               GGCCGGGGACTCCAAGTCCGGGGGCAGCGGCAGCGAATCGGACCACACCACACGCAGCAG
Sbjct:  1787 GGCCGGGGACTCCAAGTCCGGGGGCAGCGGCAGCGAATCGGACCACACCACACGCAGCAG 1846

Query:  1523 CCTGCGGGGGCCGCGGGAGCGGGCGCCCAGCGAGCGCTCAGGGCCGGCGGCCAGCGAGCA 1582
```

```
            CCTGCGGGGGCCGCGGGAGCGGGCGCCCAGCGAGCGCTCAGGGCCGGCGGCCAGCGAGCA
Sbjct:  1847 CCTGCGGGGGCCGCGGGAGCGGGCGCCCAGCGAGCGCTCAGGGCCGGCGGCCAGCGAGCA 1906

Query:  1583 CAGCCACCGCAGCCACCATTCCCTGGCCAGCAGCCTTCGCAGCCACCACACACACCCGAG 1642
            CAGCCACCGCAGCCACCATTCCCTGGCCAGCAGCCTTCGCAGCCACCACACACACCCGAG
Sbjct:  1907 CAGCCACCGCAGCCACCATTCCCTGGCCAGCAGCCTTCGCAGCCACCACACACACCCGAG 1966

Query:  1643 CTACGGTCCTCCCGGAGTGCCCCCTCTCTACGGCCCCCCCATGCTGATGATGCCCCCGCC 1702
            CTACGGTCCTCCCGGAGTGCCCCCTCTCTACGGCCCCCCCATGCTGATGATGCCCCCGCC
Sbjct:  1967 CTACGGTCCTCCCGGAGTGCCCCCTCTCTACGGCCCCCCCATGCTGATGATGCCCCCGCC 2026

Query:  1703 GCCCGCGGCCATGGGGCCCCCAGGAGCCCCTCCGGGCCGCGACCTGGCCTCAGTGCCCCC 1762
            GCCCGCGGCCATGGGGCCCCCAGGAGCCCCTCCGGGCCGCGACCTGGCCTCAGTGCCCCC
Sbjct:  2027 GCCCGCGGCCATGGGGCCCCCAGGAGCCCCTCCGGGCCGCGACCTGGCCTCAGTGCCCCC 2086

Query:  1763 GGAACTGACCGCCAGCAGACAGTCCTTCCGCATGGCCATGGGAAACCCCAGTGAGTTCTT 1822
            GGAACTGACCGCCAGCAGACAGTCCTTCCGCATGGCCATGGGAAACCCCAGTGAGTTCTT
Sbjct:  2087 GGAACTGACCGCCAGCAGACAGTCCTTCCGCATGGCCATGGGAAACCCCAGTGAGTTCTT 2146

Query:  1823 TGTGGATGTGATGTGAGCAGGGCCCCTCCCCCAGCTCCATTCCGCTCCCACCCCAGCCGG 1882
            TGTGGATGTGATGTGAGCAGGGCCCCTCCCCCAGCTCCATTCCGCTCCCACCCCAGCCGG
Sbjct:  2147 TGTGGATGTGATGTGAGCAGGGCCCCTCCCCCAGCTCCATTCCGCTCCCACCCCAGCCGG 2206

Query:  1883 CTGCGTTCCTCTCTCCATCCGTCCGTCTTTTTTACTTTGTCTGGTACCTGAAAGGGAAAT 1942
            CTGCGTTCCTCTCTCCATCCGTCCGTCTTTTTTACTTTGTCTGGTACCTGAAAGGGAAAT
Sbjct:  2207 CTGCGTTCCTCTCTCCATCCGTCCGTCTTTTTTACTTTGTCTGGTACCTGAAAGGGAAAT 2266

Query:  1943 AAAAGGAACTAAATCCA 1959
            AAAAGGAACTAAATCCA
Sbjct:  2267 AAAAGGAACTAAATCCA 2283
```

Score = 3951 (592.8 bits), Expect = 1.0e-172, P = 1.0e-172
Identities = 795/801 (99%), Positives = 795/801 (99%), Strand = Plus / Plus

```
Query:    40 AGGCCAGAGCCATGGGCGAGACCAAGATCATCTACCACTTGGATGGGCAGGAGACGCCGT 99
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:     1 AGGCCAGAGCCATGGGCGAGACCAAGATCATCTACCACTTGGATGGGCAGGAGACGCCGT 60

Query:   100 ACCTTGTGAAGCTGCCCCTGCCCGCCGAGCGCGTCACCTTGGCGGACTTTAAGGGCGTTT 159
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:    61 ACCTTGTGAAGCTGCCCCTGCCCGCCGAGCGCGTCACCTTGGCGGACTTTAAGGGCGTTT 120

Query:   160 TGCAGCGACCCAGCTATAAGTTCTTCTTCAAGTCTATGGACGACGATTTCGGAGTGGTGA 219
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   121 TGCAGCGACCCAGCTATAAGTTCTTCTTCAAGTCTATGGACGACGATTTCGGAGTGGTGA 180

Query:   220 AGGAGGAGATCTCGGATGACAATGCCAAGCTACCATGCTTCAATGGCCGGGTGGTGTCCT 279
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   181 AGGAGGAGATCTCGGATGACAATGCCAAGCTACCATGCTTCAATGGCCGGGTGGTGTCCT 240

Query:   280 GGCTGGTGTCAGCTGAGGGCTCACACCCAGACCCAGCCCCCTTCTGTGCTGATAACCCAT 339
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   241 GGCTGGTGTCAGCTGAGGGCTCACACCCAGACCCAGCCCCCTTCTGTGCTGATAACCCAT 300

Query:   340 CGGAGCTGCCACCACCTATGGAGCGCACGGGAGGCATCGGGGACTCCCGACCCCCATCCT 399
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   301 CGGAGCTGCCACCACCTATGGAGCGCACGGGAGGCATCGGGGACTCCCGACCCCCATCCT 360
```

```
Query:   400 TCCACCCTCATGCTGGTGGGGGCAGCCAGGAGAACCTGGACAATGACACAGAGACGGACT 459
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   361 TCCACCCTCATGCTGGTGGGGGCAGCCAGGAGAACCTGGACAATGACACAGAGACGGACT 420

Query:   460 CTTTGGTGTCTGCCCAGCGAGGGCGGCCACGCCGGAGGGATGGCCCAGAGCATGCAACCC 519
             |||||||||||||||||||| ||||||||||||||||||||||||||||||||||||||
Sbjct:   421 CTTTGGTGTCTGCCCAGCGAGAGCGGCCACGCCGGAGGGATGGCCCAGAGCATGCAACCC 480

Query:   520 GGCTAAATGGAACTGCGAAGGGGGAACGGCGGCGAGGACCAGGGGGTTATGATAGCTCAT 579
             |||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||
Sbjct:   481 GGCTAAATGGAACTGCGAAGGGGGAACGGCGGCGAGAACCAGGGGGTTATGATAGCTCAT 540

Query:   580 CCACCCTTATGAGCAGTGAGCTGGAGACCACCAGCTTCTTTGACTCAGATGAGGATGACT 639
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   541 CCACCCTTATGAGCAGTGAGCTGGAGACCACCAGCTTCTTTGACTCAGATGAGGATGACT 600

Query:   640 CCACCAGCAGGTTCAGCAGCTCCACAGAACAGAGCAGTGCCTCACGCCTGATGAGAAGAC 699
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   601 CCACCAGCAGGTTCAGCAGCTCCACAGAACAGAGCAGTGCCTCACGCCTGATGAGAAGAC 660

Query:   700 ACAAGCGGCGGCGGCGGAAGCAGAAGGTTTCTCGGATTGAGCGGTCCTCGTCCTTCAGCA 759
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   661 ACAAGCGGCGGCGGCGGAAGCAGAAGGTTTCTCGGATTGAGCGGTCCTCGTCCTTCAGCA 720

Query:   760 GCATCACGGACTCCACCATGTCACTCAACATCATCACGGTCACTCTCAACATGGAAAAAT 819
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   721 GCATCACGGACTCCACCATGTCACTCAACATCATCACGGTCACTCTCAACATGGAAAAAT 780

Query:   820 ATAACTTCTTGAGCACCATCA 840
             |||||||||||  |||  |  ||
Sbjct:   781 ATAACTTCTTGGGCATCTCCA 801
```

Figure 3B. BLASTP search using the protein of CuraGen Acc. No. CG164330-01.

```
>ptnr:SWISSPROT-ACC:Q92997 Segment polarity protein dishevelled homolog DVL-3
            (Dishevelled-3) (DSH homolog 3) - Homo sapiens (Human), 716 aa.
            Length = 716

 Score = 1811 (637.5 bits), Expect = 0.0, Sum P(2) = 0.0
 Identities = 336/336 (100%), Positives = 336/336 (100%)

Query:   260 LSTITSTSSSITSSIPDTERLDDFHLSIHSDMAAIVKAMASPESGLEVRDRMWLKITIPN 319
             LSTITSTSSSITSSIPDTERLDDFHLSIHSDMAAIVKAMASPESGLEVRDRMWLKITIPN
Sbjct:   381 LSTITSTSSSITSSIPDTERLDDFHLSIHSDMAAIVKAMASPESGLEVRDRMWLKITIPN 440

Query:   320 AFIGSDVVDWLYHNVEGFTDRREARKYASNLLKAGFIRHTVNKITFSEQCYYIFGDLCGN 379
             AFIGSDVVDWLYHNVEGFTDRREARKYASNLLKAGFIRHTVNKITFSEQCYYIFGDLCGN
Sbjct:   441 AFIGSDVVDWLYHNVEGFTDRREARKYASNLLKAGFIRHTVNKITFSEQCYYIFGDLCGN 500

Query:   380 MANLSLHDHDGSSGASDQDTLAPLPHPGAAPWPMAFPYQYPPPPHPYNPHPGFPPELGYSY 439
             MANLSLHDHDGSSGASDQDTLAPLPHPGAAPWPMAFPYQYPPPPHPYNPHPGFPPELGYSY
Sbjct:   501 MANLSLHDHDGSSGASDQDTLAPLPHPGAAPWPMAFPYQYPPPPHPYNPHPGFPPELGYSY 560

Query:   440 GGGSASSQHSEGSRSSGSNRSGSDRRKEKDPKAGDSKSGGSGSESDHTTRSSLRGPRERA 499
             GGGSASSQHSEGSRSSGSNRSGSDRRKEKDPKAGDSKSGGSGSESDHTTRSSLRGPRERA
Sbjct:   561 GGGSASSQHSEGSRSSGSNRSGSDRRKEKDPKAGDSKSGGSGSESDHTTRSSLRGPRERA 620
```

```
Query:   500 PSERSGPAASEHSHRSHHSLASSLRSHHTHPSYGPPGVPPLYGPPMLMMPPPPAAMGPPG 559
             PSERSGPAASEHSHRSHHSLASSLRSHHTHPSYGPPGVPPLYGPPMLMMPPPPAAMGPPG
Sbjct:   621 PSERSGPAASEHSHRSHHSLASSLRSHHTHPSYGPPGVPPLYGPPMLMMPPPPAAMGPPG 680

Query:   560 APPGRDLASVPPELTASRQSFRMAMGNPSEFFVDVM 595
             APPGRDLASVPPELTASRQSFRMAMGNPSEFFVDVM
Sbjct:   681 APPGRDLASVPPELTASRQSFRMAMGNPSEFFVDVM 716

 Score = 1340 (471.7 bits), Expect = 0.0, Sum P(2) = 0.0
 Identities = 258/260 (99%), Positives = 258/260 (99%)

Query:     1 MGETKIIYHLDGQETPYLVKLPLPAERVTLADFKGVLQRPSYKFFFKSMDDDFGVVKEEI 60
             MGETKIIYHLDGQETPYLVKLPLPAERVTLADFKGVLQRPSYKFFFKSMDDDFGVVKEEI
Sbjct:     1 MGETKIIYHLDGQETPYLVKLPLPAERVTLADFKGVLQRPSYKFFFKSMDDDFGVVKEEI 60

Query:    61 SDDNAKLPCFNGRVVSWLVSAEGSHPDPAPFCADNPSELPPPMERTGGIGDSRPPSFHPH 120
             SDDNAKLPCFNGRVVSWLVSAEGSHPDPAPFCADNPSELPPPMERTGGIGDSRPPSFHPH
Sbjct:    61 SDDNAKLPCFNGRVVSWLVSAEGSHPDPAPFCADNPSELPPPMERTGGIGDSRPPSFHPH 120

Query:   121 AGGGSQENLDNDTETDSLVSAQRGRPRRRDGPEHATRLNGTAKGERRRGPGGYDSSSTLM 180
             AGGGSQENLDNDTETDSLVSAQR RPRRRDGPEHATRLNGTAKGERRR PGGYDSSSTLM
Sbjct:   121 AGGGSQENLDNDTETDSLVSAQRERPRRRDGPEHATRLNGTAKGERRREPGGYDSSSTLM 180

Query:   181 SSELETTSFFDSDEDDSTSRFSSSTEQSSASRLMRRHKRRRRKQKVSRIERSSSFSSITD 240
             SSELETTSFFDSDEDDSTSRFSSSTEQSSASRLMRRHKRRRRKQKVSRIERSSSFSSITD
Sbjct:   181 SSELETTSFFDSDEDDSTSRFSSSTEQSSASRLMRRHKRRRRKQKVSRIERSSSFSSITD 240

Query:   241 STMSLNIITVTLNMEKYNFL 260
             STMSLNIITVTLNMEKYNFL
Sbjct:   241 STMSLNIITVTLNMEKYNFL 260
```

Figure 3C. BLASTN identity search of CuraGen Corporation's Human SeqCalling database using CuraGen Acc. No. CG164330-01.

```
>s3aq:239634112 , 5183 bp.
            Length = 5183

  Minus Strand HSPs:

 Score = 9052 (1358.2 bits), Expect = 0.0, Sum P(2) = 0.0
 Identities = 2004/2176 (92%), Positives = 2004/2176 (92%), Strand = Minus /
Plus

Query:  2634 GGTAAATTGGGGGAGGAAAAAAGAAAGAAAAGAAATGTTTCAGGCCTGGAGGTGAGATGA 2575
             GGTAAATTGGGGGAGGAAAAAAGAAAGAAAAGAAATGTTTCAGGCCTGGAGGTGAGATGA
Sbjct:  2083 GGTAAATTGGGGGAGGAAAAAAGAAAGAAAAGAAATGTTTCAGGCCTGGAGGTGAGATGA 2142

Query:  2574 GCCTGCTGGTTAGTAGGGTTAGGGGTCTGAAGGAACCAGCACGCAGGGCAGGCATGGGGC 2515
             GCCTGCTGGTTAGTAGGGTTAGGGGTCTGAAGGAACCAGCACGCAGGGCAGGCATGGGGC
Sbjct:  2143 GCCTGCTGGTTAGTAGGGTTAGGGGTCTGAAGGAACCAGCACGCAGGGCAGGCATGGGGC 2202

Query:  2514 AGGGGTAGAGCAGAGATGCTCCCTGGAAGCCACCAGCTGCTCAGGCAACTGAGGGGGCCC 2455
             AGGGGTAGAGCAGAGATGCTCCCTGGAAGCCACCAGCTGCTCAGGCAACTGAGGGGGCCC
Sbjct:  2203 AGGGGTAGAGCAGAGATGCTCCCTGGAAGCCACCAGCTGCTCAGGCAACTGAGGGGGCCC 2262

Query:  2454 TCTGGGCCTCTGATCTAGGCACAGGCAGGGATGGCATGGATGGCTATTGGAGGCGACTAC 2395
             TCTGGGCCTCTGATCTAGGCACAGGCAGGGATGGCATGGATGGCTATTGGAGGCGACTAC
```

```
Sbjct:  2263 TCTGGGCCTCTGATCTAGGCACAGGCAGGGATGGCATGGATGGCTATTGGAGGCGACTAC 2322

Query:  2394 AGCTTTAGGTTGCAGGACTGAGGCAGCAGGCAGGGGGATGGTTAGTAGGGGCAGATGAAG 2335
             AGCTTTAGGTTGCAGGACTGAGGCAGCAGGCAGGGGGATGGTTAGTAGGGGCAGATGAAG
Sbjct:  2323 AGCTTTAGGTTGCAGGACTGAGGCAGCAGGCAGGGGGATGGTTAGTAGGGGCAGATGAAG 2382

Query:  2334 CAAATATATTTTGGTTTCAGTAATGTGGGGTAAAGTCAAGAGGTTTGCACACGTGCCTGA 2275
             CAAATATATTTTGGTTTCAGTAATGTGGGGTAAAGTCAAGAGGTTTGCACACGTGCCTGA
Sbjct:  2383 CAAATATATTTTGGTTTCAGTAATGTGGGGTAAAGTCAAGAGGTTTGCACACGTGCCTGA 2442

Query:  2274 TGGGGTGGGGTTAATAGAGGGATGATGTAGCTGAATAAATGGTGAAAGGGAGCTAAAGGG 2215
             TGGGGTGGGGTTAATAGAGGGATGATGTAGCTGAATAAATGGTGAAAGGGAGCTAAAGGG
Sbjct:  2443 TGGGGTGGGGTTAATAGAGGGATGATGTAGCTGAATAAATGGTGAAAGGGAGCTAAAGGG 2502

Query:  2214 GAAACGAGAGAATGAGGGAGTGAGCGTGCCACCAAGGTCATTGCTGGGGTCAACTCCCAA 2155
             GAAACGAGAGAATGAGGGAGTGAGCGTGCCACCAAGGTCATTGCTGGGGTCAACTCCCAA
Sbjct:  2503 GAAACGAGAGAATGAGGGAGTGAGCGTGCCACCAAGGTCATTGCTGGGGTCAACTCCCAA 2562

Query:  2154 AATGGGGGTTGCAGAGGGGAGTAAGGGGTAGCACCAACAAGTCTGGTCCCAGAGACAAAA 2095
             AATGGGGGTTGCAGAGGGGAGTAAGGGGTAGCACCAACAAGTCTGGTCCCAGAGACAAAA
Sbjct:  2563 AATGGGGGTTGCAGAGGGGAGTAAGGGGTAGCACCAACAAGTCTGGTCCCAGAGACAAAA 2622

Query:  2094 GGGGTCCTGGGAAGTCCTGCGCAGGGATTAGTGGGCAGAGGAAACGAACTGGGGCCAGAG 2035
             GGGGTCCTGGGAAGTCCTGCGCAGGGATTAGTGGGCAGAGGAAACGAACTGGGGCCAGAG
Sbjct:  2623 GGGGTCCTGGGAAGTCCTGCGCAGGGATTAGTGGGCAGAGGAAACGAACTGGGGCCAGAG 2682

Query:  2034 GCAGGTTAGGGGGCTGCAGAGCCAATCGGTAGGTGCACCCCACCCTCGCAGCACCCTGCG 1975
             GCAGGTTAGGGGGCTGCAGAGCCAATCGGTAGGTGCACCCCACCCTCGCAGCACCCTGCG
Sbjct:  2683 GCAGGTTAGGGGGCTGCAGAGCCAATCGGTAGGTGCACCCCACCCTCGCAGCACCCTGCG 2742

Query:  1974 AGCAGTTAGCGCACCTGGATTTAGTTCCTTTTATTTCCCTTTCAGGTACCAGACAAAGTA 1915
             AGCAGTTAGCGCACCTGGATTTAGTTCCTTTTATTTCCCTTTCAGGTACCAGACAAAGTA
Sbjct:  2743 AGCAGTTAGCGCACCTGGATTTAGTTCCTTTTATTTCCCTTTCAGGTACCAGACAAAGTA 2802

Query:  1914 AAAAAGACGGACGGATGGAGAGAGGAACGCAGCCGGCTGGGGTGGGAGCGGAATGGAGCT 1855
             AAAAAGACGGACGGATGGAGAGAGGAACGCAGCCGGCTGGGGTGGGAGCGGAATGGAGCT
Sbjct:  2803 AAAAAGACGGACGGATGGAGAGAGGAACGCAGCCGGCTGGGGTGGGAGCGGAATGGAGCT 2862

Query:  1854 GGGGGAGGGGCCCTGCTCACATCACATCCACAAAGAACTCACTGGGGTTTCCCATGGCCA 1795
             GGGGGAGGGGCCCTGCTCACATCACATCCACAAAGAACTCACTGGGGTTTCCCATGGCCA
Sbjct:  2863 GGGGGAGGGGCCCTGCTCACATCACATCCACAAAGAACTCACTGGGGTTTCCCATGGCCA 2922

Query:  1794 TGCGGAAGGACTGTCTGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGTCGCGGCCCG 1735
             TGCGGAAGGACTGTCTGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGTCGCGGCCCG
Sbjct:  2923 TGCGGAAGGACTGTCTGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGTCGCGGCCCG 2982

Query:  1734 GAGGGGCTCCTGGGGGCCCCATGGCCGCGGGCGGCGGGGGCATCATCAGCATGGGGGGGC 1675
             GAGGGGCTCCTGGGGGCCCCATGGCCGCGGGCGGCGGGGGCATCATCAGCATGGGGGGGC
Sbjct:  2983 GAGGGGCTCCTGGGGGCCCCATGGCCGCGGGCGGCGGGGGCATCATCAGCATGGGGGGGC 3042

Query:  1674 CGTAGAGAGGGGGCACTCCGGGAGGACCGTAGCTCGGGTGTGTGTGGTGGCTGCGAAGGC 1615
             CGTAGAGAGGGGGCACTCCGGGAGGACCGTAGCTCGGGTGTGTGTGGTGGCTGCGAAGGC
Sbjct:  3043 CGTAGAGAGGGGGCACTCCGGGAGGACCGTAGCTCGGGTGTGTGTGGTGGCTGCGAAGGC 3102

Query:  1614 TGCTGGCCAGGGAATGGTGGCTGCGGTGGCTGTGCTCGCTGGCCGCCGGCCCTGAGCGCT 1555
             TGCTGGCCAGGGAATGGTGGCTGCGGTGGCTGTGCTCGCTGGCCGCCGGCCCTGAGCGCT
Sbjct:  3103 TGCTGGCCAGGGAATGGTGGCTGCGGTGGCTGTGCTCGCTGGCCGCCGGCCCTGAGCGCT 3162
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Query:  1554 CGCTGGGCGCCCGCTCCCGCGGCCCCCGCAGGCTGCTGCGTGTGGTGTGGTCCGATTCGC 1495
             CGCTGGGCGCCCGCTCCCGCGGCCCCCGCAGGCTGCTGCGTGTGGTGTGGTCCGATTCGC
Sbjct:  3163 CGCTGGGCGCCCGCTCCCGCGGCCCCCGCAGGCTGCTGCGTGTGGTGTGGTCCGATTCGC 3222

Query:  1494 TGCCGCTGCCCCCGGACTTGGAGTCCCCGGCCTTCGGGTCCTTCTCCTTCCTCCGATCGC 1435
             TGCCGCTGCCCCCGGACTTGGAGTCCCCGGCCTTCGGGTCCTTCTCCTTCCTCCGATCGC
Sbjct:  3223 TGCCGCTGCCCCCGGACTTGGAGTCCCCGGCCTTCGGGTCCTTCTCCTTCCTCCGATCGC 3282

Query:  1434 TGCCGCTACGGTTGGAGCCACTGCTCCGACTGCCTTCGCTGTGCTGACTGCTGGCGCTGC 1375
             TGCCGCTACGGTTGGAGCCACTGCTCCGACTGCCTTCGCTGTGCTGACTGCTGGCGCTGC
Sbjct:  3283 TGCCGCTACGGTTGGAGCCACTGCTCCGACTGCCTTCGCTGTGCTGACTGCTGGCGCTGC 3342

Query:  1374 CCCCGCCGTAGCTGTAGCCCAGCTCCGGGAAGCCCGGGTGCGGGTTGTATGGGTGCGGGG 1315
             CCCCGCCGTAGCTGTAGCCCAGCTCCGGGAAGCCCGGGTGCGGGTTGTATGGGTGCGGGG
Sbjct:  3343 CCCCGCCGTAGCTGTAGCCCAGCTCCGGGAAGCCCGGGTGCGGGTTGTATGGGTGCGGGG 3402

Query:  1314 GTGGCGGGTACTGGTACGGGAAAGCCATGGGCCAAGGGGCGGCCCCCGGGTGCGGCAAAG 1255
             GTGGCGGGTACTGGTACGGGAAAGCCATGGGCCAAGGGGCGGCCCCCGGGTGCGGCAAAG
Sbjct:  3403 GTGGCGGGTACTGGTACGGGAAAGCCATGGGCCAAGGGGCGGCCCCCGGGTGCGGCAAAG 3462

Query:  1254 GGGCCAGTGTGTCCTGGTCAGAGGCGCCACTGGAGCCATCGTGATCGTGGAGAGACAGGT 1195
             GGGCCAGTGTGTCCTGGTCAGAGGCGCCACTGGAGCCATCGTGATCGTGGAGAGACAGGT
Sbjct:  3463 GGGCCAGTGTGTCCTGGTCAGAGGCGCCACTGGAGCCATCGTGATCGTGGAGAGACAGGT 3522

Query:  1194 TGGCCATGTTGCCGCAGAGGTCACCGAAGATGTAGTAGCACTGCTCGGAGAAGGTGATCT 1135
             TGGCCATGTTGCCGCAGAGGTCACCGAAGATGTAGTAGCACTGCTCGGAGAAGGTGATCT
Sbjct:  3523 TGGCCATGTTGCCGCAGAGGTCACCGAAGATGTAGTAGCACTGCTCGGAGAAGGTGATCT 3582

Query:  1134 TGTTGACGGTATGGCGGATGAAGCCAGCTTTCAGCAGGTTGCTGGCATACTTGCGGGCCT 1075
             TGTTGACGGTATGGCGGATGAAGCCAGCTTTCAGCAGGTTGCTGGCATACTTGCGGGCCT
Sbjct:  3583 TGTTGACGGTATGGCGGATGAAGCCAGCTTTCAGCAGGTTGCTGGCATACTTGCGGGCCT 3642

Query:  1074 CCCTCCGGTCCGTGAAGCCTTCCACATTGTGGTACAGCCAGTCCACCACATCTGAGCCGA 1015
             CCCTCCGGTCCGTGAAGCCTTCCACATTGTGGTACAGCCAGTCCACCACATCTGAGCCGA
Sbjct:  3643 CCCTCCGGTCCGTGAAGCCTTCCACATTGTGGTACAGCCAGTCCACCACATCTGAGCCGA 3702

Query:  1014 TGAAAGCATTAGGGATGGTAATCTTGAGCCACATGCGGTCACGGACCTCCAACCCTGATT 955
             TGAAAGCATTAGGGATGGTAATCTTGAGCCACATGCGGTCACGGACCTCCAACCCTGATT
Sbjct:  3703 TGAAAGCATTAGGGATGGTAATCTTGAGCCACATGCGGTCACGGACCTCCAACCCTGATT 3762

Query:   954 CAGGGGAGGCCATGGCTTTTACGATGGCAGCCATGTCACTGTGGATGGACAAGTGGAAGT 895
             CAGGGGAGGCCATGGCTTTTACGATGGCAGCCATGTCACTGTGGATGGACAAGTGGAAGT
Sbjct:  3763 CAGGGGAGGCCATGGCTTTTACGATGGCAGCCATGTCACTGTGGATGGACAAGTGGAAGT 3822

Query:   894 CGTCTAGGCGCTCTGTGTCAGGGATGGAACTGGTGATGGAGGAGCTGGTGGAGGTGATGG 835
             CGTCTAGGCGCTCTGTGTCAGGGATGGAACTGGTGATGGAGGAGCTGGTGGAGGTGATGG
Sbjct:  3823 CGTCTAGGCGCTCTGTGTCAGGGATGGAACTGGTGATGGAGGAGCTGGTGGAGGTGATGG 3882

Query:   834 TGCTCAAGAAGTTATATTTTTCCATGTTGAGAGTGACCGTGATGATGTTGAGTGACATGG 775
             TGCTCA G AG     T  T CC T T  AG G GA  GTG  G T  TG  TG CA  G
Sbjct:  3883 TGCTCAGGGAGGGGC-TCATGCCGTATGCAG-G-GAAGGTGCCGGTCATGGCTG-CAGTG 3938

Query:   774 TGG-AGTCCGTGAT-GCTGC-TGAA-GGACGAGGACCG-CTCAATCC-GAGAAACCTTCT 721
             TGG AG CC  G   GC G  T AA GG C  GGA  G CTC  TCC G G AA  T
Sbjct:  3939 TGGGAGACCCAGGCCGCAGGGTCAATGGGCC-GGATGGGCTCGCTCCTGGGCAATGTGAA 3997

Query:   720 GCTTCCGCCGCCGCCGCTTGTGTCTTCTCATCAGGCGTGAGGCACTGCTCTGTTCTGTGG 661
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            GC  CC C G  G C  TTG GTC    CA   GGC   AG CA  G   TG  C   GG
Sbjct:  3998 GCAACCAC-GTGGAC--TTGGGTCCCAGCACTTGGCTACAGTCAGGGTGATGGGCCCCGG 4054

Query:   660 AGCTGCTGAACCTGCTGGTGGAGTCATCCTCATCTGAGTCAA-AGAAGCTGGTGGTCTCC 602
               TG TG AC   CT   G AGT A CC  A CTG  TC   A  A CT  TG TCTC
Sbjct:  4055 TT-TG-TGCACAATCTCCCGCAGT-ACCCGGA-CTGCATCGTCATTA-CTCATGTTCTCA 4109

Query:   601 A-GCTCACTGCTCATAAGGGTGGATGAGC-TATCA--TAACCCCCTG-GTCC-TC-GCCG 549
           A G T A T CTC T     TG A  A C TATC   T  C C  TG GTCC TC GC G
Sbjct:  4110 AAGTTGA-T-CTCGTTTACCTGTAACAACATATCTCCTGGCTCGATGCGTCCATCAGCAG 4167

Query:   548 CCGTTCCCCCTTCGCAGTTCCATTTAGCCGG-GTTGCATGCTCTGGGCCATCCCTC-CGG 491
           CC    CCCC  C     T  AT  AGCC   GT G ATGC C   G CA C C C CG
Sbjct:  4168 CCACGGCCCCACCCTTCATG-ATAGAGCCAATGTAG-ATGC-CGCCGTCACCACGCTCGT 4224

Query:   490 CGTGGCCGCCCTCGCTGGGCAGACACCAAAGA 459
              G     GCCC C  TGG  AGA  CC AAGA
Sbjct:  4225 TGCTTTGGCCCACAATGG--AGATGCCCAAGA 4254

 Score = 2162 (324.4 bits), Expect = 1.2e-182, Sum P(3) = 1.2e-182
 Identities = 466/486 (95%), Positives = 466/486 (95%), Strand = Minus / Plus

Query:   840 TGATGGTGCTCAAGAAGTTATATTTTTCCATGTTGAGAGTGACCGTGATGATGTTGAGTG 781
           TG  G TGC CAAGAAGTTATATTTTTCCATGTTGAGAGTGACCGTGATGATGTTGAGTG
Sbjct:  4240 TGGAGATGCCCAAGAAGTTATATTTTTCCATGTTGAGAGTGACCGTGATGATGTTGAGTG 4299

Query:   780 ACATGGTGGAGTCCGTGATGCTGCTGAAGGACGAGGACCGCTCAATCCGAGAAACCTTCT 721
           ACATGGTGGAGTCCGTGATGCTGCTGAAGGACGAGGACCGCTCAATCCGAGAAACCTTCT
Sbjct:  4300 ACATGGTGGAGTCCGTGATGCTGCTGAAGGACGAGGACCGCTCAATCCGAGAAACCTTCT 4359

Query:   720 GCTTCCGCCGCCGCCGCTTGTGTCTTCTCATCAGGCGTGAGGCACTGCTCTGTTCTGTGG 661
           GCTTCCGCCGCCGCCGCTTGTGTCTTCTCATCAGGCGTGAGGCACTGCTCTGTTCTGTGG
Sbjct:  4360 GCTTCCGCCGCCGCCGCTTGTGTCTTCTCATCAGGCGTGAGGCACTGCTCTGTTCTGTGG 4419

Query:   660 AGCTGCTGAACCTGCTGGTGGAGTCATCCTCATCTGAGTCAAAGAAGCTGGTGGTCTCCA 601
           AGCTGCTGAACCTGCTGGTGGAGTCATCCTCATCTGAGTCAAAGAAGCTGGTGGTCTCCA
Sbjct:  4420 AGCTGCTGAACCTGCTGGTGGAGTCATCCTCATCTGAGTCAAAGAAGCTGGTGGTCTCCA 4479

Query:   600 GCTCACTGCTCATAAGGGTGGATGAGCTATCATAACCCCCTGGTCCTCGCCGCCGTTCCC 541
           GCTCACTGCTCATAAGGGTGGATGAGCTATCATAACCCCCTGGT CTCGCCGCCGTTCCC
Sbjct:  4480 GCTCACTGCTCATAAGGGTGGATGAGCTATCATAACCCCCTGGTTCTCGCCGCCGTTCCC 4539

Query:   540 CCTTCGCAGTTCCATTTAGCCGGGTTGCATGCTCTGGGCCATCCCTCCGGCGTGGCCGCC 481
           CCTTCGCAGTTCCATTTAGCCGGGTTGCATGCTCTGGGCCATCCCTCCGGCGTGGCCGCC
Sbjct:  4540 CCTTCGCAGTTCCATTTAGCCGGGTTGCATGCTCTGGGCCATCCCTCCGGCGTGGCCGCC 4599

Query:   480 CTCGCTGGGCAGACACCAAAGAGTCCGTCTCTGTGTCATTGTCCAGGTTCTCCTGGCTGC 421
           CTCGCTGGGCAGACACCAAAGAGTCCGTCTCTGTGTCATTGTCCAGGTTCTCCTGGCTGC
Sbjct:  4600 CTCGCTGGGCAGACACCAAAGAGTCCGTCTCTGTGTCATTGTCCAGGTTCTCCTGGCTGC 4659

Query:   420 CCCCACCAGCATGAGGG-TG--G--AAG-GATGGG-GGTCGGGAGTCCCCGATGCCTCCC 368
           CCCCACCAGCATGAGGG TG  G  AAG GATGG  GG  GGG GTC   GA G C CCC
Sbjct:  4660 CCCCACCAGCATGAGGGCTGCAGGGAAGAGATGGAAGGATGGGGGTCGG-GA-GTC-CCC 4716

Query:   367 G-TGCGCTCC 359
           G TGC CTCC
Sbjct:  4717 GATGC-CTCC 4725
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 Score = 2018 (302.8 bits), Expect = 0.0, Sum P(2) = 0.0
 Identities = 408/412 (99%), Positives = 408/412 (99%), Strand = Minus / Plus

Query:   412 GCATGAGGGTGGAAGGATGGGGGTCGGGAGTCCCCGATGCCTCCCGTGCGCTCCATAGGT 353
             G A GAG  TGGAAGGATGGGGGTCGGGAGTCCCCGATGCCTCCCGTGCGCTCCATAGGT
Sbjct:  4683 GGAAGAGA-TGGAAGGATGGGGGTCGGGAGTCCCCGATGCCTCCCGTGCGCTCCATAGGT 4741

Query:   352 GGTGGCAGCTCCGATGGGTTATCAGCACAGAAGGGGGCTGGGTCTGGGTGTGAGCCCTCA 293
             GGTGGCAGCTCCGATGGGTTATCAGCACAGAAGGGGGCTGGGTCTGGGTGTGAGCCCTCA
Sbjct:  4742 GGTGGCAGCTCCGATGGGTTATCAGCACAGAAGGGGGCTGGGTCTGGGTGTGAGCCCTCA 4801

Query:   292 GCTGACACCAGCCAGGACACCACCCGGCCATTGAAGCATGGTAGCTTGGCATTGTCATCC 233
             GCTGACACCAGCCAGGACACCACCCGGCCATTGAAGCATGGTAGCTTGGCATTGTCATCC
Sbjct:  4802 GCTGACACCAGCCAGGACACCACCCGGCCATTGAAGCATGGTAGCTTGGCATTGTCATCC 4861

Query:   232 GAGATCTCCTCCTTCACCACTCCGAAATCGTCGTCCATAGACTTGAAGAAGAACTTATAG 173
             GAGATCTCCTCCTTCACCACTCCGAAATCGTCGTCCATAGACTTGAAGAAGAACTTATAG
Sbjct:  4862 GAGATCTCCTCCTTCACCACTCCGAAATCGTCGTCCATAGACTTGAAGAAGAACTTATAG 4921

Query:   172 CTGGGTCGCTGCAAAACGCCCTTAAAGTCCGCCAAGGTGACGCGCTCGGCGGGCAGGGGC 113
             CTGGGTCGCTGCAAAACGCCCTTAAAGTCCGCCAAGGTGACGCGCTCGGCGGGCAGGGGC
Sbjct:  4922 CTGGGTCGCTGCAAAACGCCCTTAAAGTCCGCCAAGGTGACGCGCTCGGCGGGCAGGGGC 4981

Query:   112 AGCTTCACAAGGTACGGCGTCTCCTGCCCATCCAAGTGGTAGATGATCTTGGTCTCGCCC 53
             AGCTTCACAAGGTACGGCGTCTCCTGCCCATCCAAGTGGTAGATGATCTTGGTCTCGCCC
Sbjct:  4982 AGCTTCACAAGGTACGGCGTCTCCTGCCCATCCAAGTGGTAGATGATCTTGGTCTCGCCC 5041

Query:    52 ATGGCTCTGGCCTCGGGCCCGGCGGCCCGCGCGCGGCCTGCTCGGGCGGCCG 1
             ATGGCTCTGGCCTCGGGCCCGGCGGCCCGCGCGCGGCCTGCTCGGGCGGCCG
Sbjct:  5042 ATGGCTCTGGCCTCGGGCCCGGCGGCCCGCGCGCGGCCTGCTCGGGCGGCCG 5093

 Score = 145 (21.8 bits), Expect = 1.2e-182, Sum P(3) = 1.2e-182
 Identities = 49/68 (72%), Positives = 49/68 (72%), Strand = Minus / Plus

Query:  1561 GAGCGCTCGCTGGGCGCCCGCTCCCGCGGCCCCCGCAGGCTGCTGCGTGTGGTGTGGTCC 1502
             GAG GCT     GGC CCC CTCCC C  CC CCGCAGGCTGC  C  GTGGTG G TCC
Sbjct:  1797 GAGAGCTAAAGAGGCCCCC-CTCCC-C--CCGCCGCAGGCTGCCACACGTGGTGCGATCC 1852

Query:  1501 GATTCGCT 1494
             GATTC CT
Sbjct:  1853 GATTCTCT 1860


>s3aq:220118507 , 2070 bp.
           Length = 2070

  Plus Strand HSPs:

 Score = 5677 (851.8 bits), Expect = 2.4e-251, P = 2.4e-251
 Identities = 1329/1501 (88%), Positives = 1329/1501 (88%), Strand = Plus /
Plus

Query:   459 TCTTTGGTGTCTGCCCAGCGAGGGCGGCCACGCCG-GAGGGATGGCCCAGAGCATGCAAC 517
             TCTT GG  TCT CC A  G GGGC     C  CG G G G TG C   G GCAT C AC
Sbjct:   558 TCTTGGGCATCT-CC-ATTGTGGGCCAAAGCAACGAGCGTGGTGACGGCG-GCAT-CTAC 613

Query:   518 CC-GGCTAAATGGAACTGCGAAGGGGGAACGGCGGC-GA-GGAC-CAGGGGGTTATGA-- 571
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                GGCT  AT      G G  GGGG    GGC GC GA GGAC CA  G G  A GA
Sbjct:   614 ATTGGCTCTATCATGAAGGGT-GGGGCCGTGGCTGCTGATGGACGCATCGAGCCAGGAGA 672

Query:   572 TA-GCTCATCCACCCTTATGAGCAGTGAGCTG-GAGACCACCAGCTTCTTT-GACTCAGA 628
             TA G T  T CA     A GAG A T A CT  GAGA CA  AG T  T   GA  CAG
Sbjct:   673 TATGTTGTTACAGGTAAACGAG-A-TCAACTTTGAGAACATGAG-TAATGACGATGCAG- 728

Query:   629 TGAGGATGACTCCACCAGCAGGTTCAGCAGCTCCACAGAACAGAGCAGTGCCTCACGCCT 688
             T  GG T ACT C   AG   GT CA CA   CC   G  CA   C  TG CT   GCC
Sbjct:   729 TCCGGGT-ACTGCGGGAGATTGTGCA-CAAA-CCGGGGCCCATCACCCTGACTGTAGCCA 785

Query:   689 GATGAGAAGACACAAGCGGCGGCGGCGGAAGCAGAAGGTTTCTC-GGATTGAGCGG-TCC 746
               TG    GAC CAAG   C  CG  GG  GC   A  TT C C GGA  GAGC   TCC
Sbjct:   786 AGTGCTGGGACCCAAGTC-CA-CGT-GGTTGCTTCACATTGCCCAGGAGCGAGCCCATCC 842

Query:   747 TCGTCC-TTCAGCA-GCATCACGGA-CTCCACCA-TGTCACTCAACATCATCACGGTCAC 802
               G CC TT A C  GC  C  GG  CTCC  CA TG CA  CA  A C  CAC  TC C
Sbjct:   843 G-GCCCATTGACCCTGCGGCCTGGGTCTCCCACACTG-CAGCCATGACCGGCACCTTCCC 900

Query:   803 TCTCAACATGGAAAAATATAACTTCTTGAGCACCATCACCTCCACCAGCTCCTCCATCAC 862
             T  CA  A GG A  A     CT C TGAGCACCATCACCTCCACCAGCTCCTCCATCAC
Sbjct:   901 TG-CAT-ACGGCATGAGCCC-CTCCCTGAGCACCATCACCTCCACCAGCTCCTCCATCAC 957

Query:   863 CAGTTCCATCCCTGACACAGAGCGCCTAGACGACTTCCACTTGTCCATCCACAGTGACAT 922
             CAGTTCCATCCCTGACACAGAGCGCCTAGACGACTTCCACTTGTCCATCCACAGTGACAT
Sbjct:   958 CAGTTCCATCCCTGACACAGAGCGCCTAGACGACTTCCACTTGTCCATCCACAGTGACAT 1017

Query:   923 GGCTGCCATCGTAAAAGCCATGGCCTCCCCTGAATCAGGGTTGGAGGTCCGTGACCGCAT 982
             GGCTGCCATCGTAAAAGCCATGGCCTCCCCTGAATCAGGGTTGGAGGTCCGTGACCGCAT
Sbjct:  1018 GGCTGCCATCGTAAAAGCCATGGCCTCCCCTGAATCAGGGTTGGAGGTCCGTGACCGCAT 1077

Query:   983 GTGGCTCAAGATTACCATCCCTAATGCTTTCATCGGCTCAGATGTGGTGGACTGGCTGTA 1042
             GTGGCTCAAGATTACCATCCCTAATGCTTTCATCGGCTCAGATGTGGTGGACTGGCTGTA
Sbjct:  1078 GTGGCTCAAGATTACCATCCCTAATGCTTTCATCGGCTCAGATGTGGTGGACTGGCTGTA 1137

Query:  1043 CCACAATGTGGAAGGCTTCACGGACCGGAGGGAGGCCCGCAAGTATGCCAGCAACCTGCT 1102
             CCACAATGTGGAAGGCTTCACGGACCGGAGGGAGGCCCGCAAGTATGCCAGCAACCTGCT
Sbjct:  1138 CCACAATGTGGAAGGCTTCACGGACCGGAGGGAGGCCCGCAAGTATGCCAGCAACCTGCT 1197

Query:  1103 GAAAGCTGGCTTCATCCGCCATACCGTCAACAAGATCACCTTCTCCGAGCAGTGCTACTA 1162
             GAAAGCTGGCTTCATCCGCCATACCGTCAACAAGATCACCTTCTCCGAGCAGTGCTACTA
Sbjct:  1198 GAAAGCTGGCTTCATCCGCCATACCGTCAACAAGATCACCTTCTCCGAGCAGTGCTACTA 1257

Query:  1163 CATCTTCGGTGACCTCTGCGGCAACATGGCCAACCTGTCTCTCCACGATCACGATGGCTC 1222
             CATCTTCGGTGACCTCTGCGGCAACATGGCCAACCTGTCTCTCCACGATCACGATGGCTC
Sbjct:  1258 CATCTTCGGTGACCTCTGCGGCAACATGGCCAACCTGTCTCTCCACGATCACGATGGCTC 1317

Query:  1223 CAGTGGCGCCTCTGACCAGGACACACTGGCCCCTTTGCCGCACCCGGGGGCCGCCCCTTG 1282
             CAGTGGCGCCTCTGACCAGGACACACTGGCCCCTTTGCCGCACCCGGGGGCCGCCCCTTG
Sbjct:  1318 CAGTGGCGCCTCTGACCAGGACACACTGGCCCCTTTGCCGCACCCGGGGGCCGCCCCTTG 1377

Query:  1283 GCCCATGGCTTTCCCGTACCAGTACCCGCCACCCCCGCACCCATACAACCCGCACCCGGG 1342
             GCCCATGGCTTTCCCGTACCAGTACCCGCCACCCCCGCACCCATACAACCCGCACCCGGG
Sbjct:  1378 GCCCATGGCTTTCCCGTACCAGTACCCGCCACCCCCGCACCCATACAACCCGCACCCGGG 1437

Query:  1343 CTTCCCGGAGCTGGGCTACAGCTACGGCGGGGGCAGCGCCAGCAGTCAGCACAGCGAAGG 1402
             CTTCCCGGAGCTGGGCTACAGCTACGGCGGGGGCAGCGCCAGCAGTCAGCACAGCGAAGG
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Sbjct:  1438 CTTCCCGGAGCTGGGCTACAGCTACGGCGGGGGCAGCGCCAGCAGTCAGCACAGCGAAGG 1497

Query:  1403 CAGTCGGAGCAGTGGCTCCAACCGTAGCGGCAGCGATCGGAGGAAGGAGAAGGACCCGAA 1462
             CAGTCGGAGCAGTGGCTCCAACCGTAGCGGCAGCGATCGGAGGAAGGAGAAGGACCCGAA
Sbjct:  1498 CAGTCGGAGCAGTGGCTCCAACCGTAGCGGCAGCGATCGGAGGAAGGAGAAGGACCCGAA 1557

Query:  1463 GGCCGGGGACTCCAAGTCCGGGGGCAGCGGCAGCGAATCGGACCACACCACACGCAGCAG 1522
             GGCCGGGGACTCCAAGTCCGGGGGCAGCGGCAGCGAATCGGACCACACCACACGCAGCAG
Sbjct:  1558 GGCCGGGGACTCCAAGTCCGGGGGCAGCGGCAGCGAATCGGACCACACCACACGCAGCAG 1617

Query:  1523 CCTGCGGGGGCCGCGGGAGCGGGCGCCCAGCGAGCGCTCAGGGCCGGCGGCCAGCGAGCA 1582
             CCTGCGGGGGCCGCGGGAGCGGGCGCCCAGCGAGCGCTCAGGGCCGGCGGCCAGCGAGCA
Sbjct:  1618 CCTGCGGGGGCCGCGGGAGCGGGCGCCCAGCGAGCGCTCAGGGCCGGCGGCCAGCGAGCA 1677

Query:  1583 CAGCCACCGCAGCCACCATTCCCTGGCCAGCAGCCTTCGCAGCCACCACACACACCCGAG 1642
             CAGCCACCGCAGCCACCATTCCCTGGCCAGCAGCCTTCGCAGCCACCACACACACCCGAG
Sbjct:  1678 CAGCCACCGCAGCCACCATTCCCTGGCCAGCAGCCTTCGCAGCCACCACACACACCCGAG 1737

Query:  1643 CTACGGTCCTCCCGGAGTGCCCCCTCTCTACGGCCCCCCCATGCTGATGATGCCCCCGCC 1702
             CTACGGTCCTCCCGGAGTGCCCCCTCTCTACGGCCCCCCCATGCTGATGATGCCCCCGCC
Sbjct:  1738 CTACGGTCCTCCCGGAGTGCCCCCTCTCTACGGCCCCCCCATGCTGATGATGCCCCCGCC 1797

Query:  1703 GCCCGCGGCCATGGGGCCCCCAGGAGCCCCTCCGGGCCGCGACCTGGCCTCAGTGCCCCC 1762
             GCCCGCGGCCATGGGGCCCCCAGGAGCCCCTCCGGGCCGCGACCTGGCCTCAGTGCCCCC
Sbjct:  1798 GCCCGCGGCCATGGGGCCCCCAGGAGCCCCTCCGGGCCGCGACCTGGCCTCAGTGCCCCC 1857

Query:  1763 GGAACTGACCGCCAGCAGACAGTCCTTCCGCATGGCCATGGGAAACCCCAGTGAGTTCTT 1822
             GGAACTGACCGCCAGCAGACAGTCCTTCCGCATGGCCATGGGAAACCCCAGTGAGTTCTT
Sbjct:  1858 GGAACTGACCGCCAGCAGACAGTCCTTCCGCATGGCCATGGGAAACCCCAGTGAGTTCTT 1917

Query:  1823 TGTGGATGTGATGTGAGCAGGGCCCCTCCCCCAGCTCCATTCCGCTCCCACCCCAGCCGG 1882
             TGTGGATGTGATGTGAGCAGGGCCCCTCCCCCAGCTCCATTCCGCTCCCACCCCAGCCGG
Sbjct:  1918 TGTGGATGTGATGTGAGCAGGGCCCCTCCCCCAGCTCCATTCCGCTCCCACCCCAGCCGG 1977

Query:  1883 CTGCGTTCCTCTCTCCATCCGTCCGTCTTTTTTACTTTGTCTGGTACCTGAAAGGGAAAT 1942
             CTGCGTTCCTCTCTCCATCCGTCCGTCTTTTTTACTTTGTCTGGTACCTGAAAGGGAAAT
Sbjct:  1978 CTGCGTTCCTCTCTCCATCCGTCCGTCTTTTTTACTTTGTCTGGTACCTGAAAGGGAAAT 2037

Query:  1943 AAAAGGAACTAAATCCA 1959
             AAAAGGAACTAAATCCA
Sbjct:  2038 AAAAGGAACTAAATCCA 2054

 Score = 992 (148.8 bits), Expect = 7.2e-73, Sum P(2) = 7.2e-73
 Identities = 200/202 (99%), Positives = 200/202 (99%), Strand = Plus / Plus

Query:   450 GAGACGGACTCTTTGGTGTCTGCCCAGCGAGGGCGGCCACGCCGGAGGGATGGCCCAGAG 509
             |||||||||||||||||||||||||||||| ||||||||||||||||||||||||||||
Sbjct:     1 GAGACGGACTCTTTGGTGTCTGCCCAGCGAGAGCGGCCACGCCGGAGGGATGGCCCAGAG 60

Query:   510 CATGCAACCCGGCTAAATGGAACTGCGAAGGGGGAACGGCGGCGAGGACCAGGGGGTTAT 569
             ||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Sbjct:    61 CATGCAACCCGGCTAAATGGAACTGCGAAGGGGGAACGGCGGCGAGAACCAGGGGGTTAT 120

Query:   570 GATAGCTCATCCACCCTTATGAGCAGTGAGCTGGAGACCACCAGCTTCTTTGACTCAGAT 629
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   121 GATAGCTCATCCACCCTTATGAGCAGTGAGCTGGAGACCACCAGCTTCTTTGACTCAGAT 180
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Query:   630 GAGGATGACTCCACCAGCAGGT 651
             |||||||||||||||||||||
Sbjct:   181 GAGGATGACTCCACCAGCAGGT 202

 Score = 940 (141.0 bits), Expect = 7.2e-73, Sum P(2) = 7.2e-73
 Identities = 194/200 (97%), Positives = 194/200 (97%), Strand = Plus / Plus

Query:   641 CACCAGCAGGTTCAGCAGCTCCACAGAACAGAGCAGTGCCTCACGCCTGATGAGAAGACA 700
             C CCA CAGGTTCAGCAGCTCCACAGAACAGAGCAGTGCCTCACGCCTGATGAGAAGACA
Sbjct:   374 CCCCA-CAGGTTCAGCAGCTCCACAGAACAGAGCAGTGCCTCACGCCTGATGAGAAGACA 432

Query:   701 CAAGCGGCGGCGGCGGAAGCAGAAGGTTTCTCGGATTGAGCGGTCCTCGTCCTTCAGCAG 760
             CAAGCGGCGGCGGCGGAAGCAGAAGGTTTCTCGGATTGAGCGGTCCTCGTCCTTCAGCAG
Sbjct:   433 CAAGCGGCGGCGGCGGAAGCAGAAGGTTTCTCGGATTGAGCGGTCCTCGTCCTTCAGCAG 492

Query:   761 CATCACGGACTCCACCATGTCACTCAACATCATCACGGTCACTCTCAACATGGAAAAATA 820
             CATCACGGACTCCACCATGTCACTCAACATCATCACGGTCACTCTCAACATGGAAAAATA
Sbjct:   493 CATCACGGACTCCACCATGTCACTCAACATCATCACGGTCACTCTCAACATGGAAAAATA 552

Query:   821 TAACTTCTTGAGCACCATCA 840
             TAACTTCTTG GCA C  CA
Sbjct:   553 TAACTTCTTGGGCATCTCCA 572


>s3aq:220119318 , 873 bp.
           Length = 873

  Plus Strand HSPs:

 Score = 4279 (642.0 bits), Expect = 7.8e-188, P = 7.8e-188
 Identities = 865/872 (99%), Positives = 865/872 (99%), Strand = Plus / Plus

Query:   362 GCGCACGGGAGGCATCGGGGACTCCCGACCCCCATCCTTCCACCCTCATGCTGGTGGGGG 421
             GC CACGG AGG ATC GGGACTCCCGACCCCCATCCTTCCACCCTCATGCTGGTGGGGG
Sbjct:     4 GCCCACGG-AGGTATCTGGGACTCCCGACCCCCATCCTTCCACCCTCATGCTGGTGGGGG 62

Query:   422 CAGCCAGGAGAACCTGGACAATGACACAGAGACGGACTCTTTGGTGTCTGCCCAGCGAGG 481
             CAGCCAGGAGAACCTGGACAATGACACAGAGACGGACTCTTTGGTGTCTGCCCAGCGAGG
Sbjct:    63 CAGCCAGGAGAACCTGGACAATGACACAGAGACGGACTCTTTGGTGTCTGCCCAGCGAGG 122

Query:   482 GCGGCCACGCCGGAGGGATGGCCCAGAGCATGCAACCCGGCTAAATGGAACTGCGAAGGG 541
             GCGGCCACGCCGGAGGGATGGCCCAGAGCATGCAACCCGGCTAAATGGAACTGCGAAGGG
Sbjct:   123 GCGGCCACGCCGGAGGGATGGCCCAGAGCATGCAACCCGGCTAAATGGAACTGCGAAGGG 182

Query:   542 GGAACGGCGGCGAGGACCAGGGGGTTATGATAGCTCATCCACCCTTATGAGCAGTGAGCT 601
             GGAACGGCGGCGAGGACCAGGGGGTTATGATAGCTCATCCACCCTTATGAGCAGTGAGCT
Sbjct:   183 GGAACGGCGGCGAGGACCAGGGGGTTATGATAGCTCATCCACCCTTATGAGCAGTGAGCT 242

Query:   602 GGAGACCACCAGCTTCTTTGACTCAGATGAGGATGACTCCACCAGCAGGTTCAGCAGCTC 661
             GGAGACCACCAGCTTCTTTGACTCAGATGAGGATGACTCCACCAGCAGGTTCAGCAGCTC
Sbjct:   243 GGAGACCACCAGCTTCTTTGACTCAGATGAGGATGACTCCACCAGCAGGTTCAGCAGCTC 302

Query:   662 CACAGAACAGAGCAGTGCCTCACGCCTGATGAGAAGACACAAGCGGCGGCGGCGGAAGCA 721
             CACAGAACAGAGCAGTGCCTCACGCCTGATGAGAAGACACAAGCGGCGGCGGCGGAAGCA
Sbjct:   303 CACAGAACAGAGCAGTGCCTCACGCCTGATGAGAAGACACAAGCGGCGGCGGCGGAAGCA 362

Query:   722 GAAGGTTTCTCGGATTGAGCGGTCCTCGTCCTTCAGCAGCATCACGGACTCCACCATGTC 781
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            GAAGGTTTCTCGGATTGAGCGGTCCTCGTCCTTCAGCAGCATCACGGACTCCACCATGTC
Sbjct:  363 GAAGGTTTCTCGGATTGAGCGGTCCTCGTCCTTCAGCAGCATCACGGACTCCACCATGTC 422

Query:  782 ACTCAACATCATCACGGTCACTCTCAACATGGAAAAATATAACTTCTTGAGCACCATCAC 841
            ACTCAACATCATCACGGTCACTCTCAACATGGAAAAATATAACTTCTTGAGCACCATCAC
Sbjct:  423 ACTCAACATCATCACGGTCACTCTCAACATGGAAAAATATAACTTCTTGAGCACCATCAC 482

Query:  842 CTCCACCAGCTCCTCCATCACCAGTTCCATCCCTGACACAGAGCGCCTAGACGACTTCCA 901
            CTCCACCAGCTCCTCCATCACCAGTTCCATCCCTGACACAGAGCGCCTAGACGACTTCCA
Sbjct:  483 CTCCACCAGCTCCTCCATCACCAGTTCCATCCCTGACACAGAGCGCCTAGACGACTTCCA 542

Query:  902 CTTGTCCATCCACAGTGACATGGCTGCCATCGTAAAAGCCATGGCCTCCCCTGAATCAGG 961
            CTTGTCCATCCACAGTGACATGGCTGCCATCGTAAAAGCCATGGCCTCCCCTGAATCAGG
Sbjct:  543 CTTGTCCATCCACAGTGACATGGCTGCCATCGTAAAAGCCATGGCCTCCCCTGAATCAGG 602

Query:  962 GTTGGAGGTCCGTGACCGCATGTGGCTCAAGATTACCATCCCTAATGCTTTCATCGGCTC 1021
            GTTGGAGGTCCGTGACCGCATGTGGCTCAAGATTACCATCCCTAATGCTTTCATCGGCTC
Sbjct:  603 GTTGGAGGTCCGTGACCGCATGTGGCTCAAGATTACCATCCCTAATGCTTTCATCGGCTC 662

Query: 1022 AGATGTGGTGGACTGGCTGTACCACAATGTGGAAGGCTTCACGGACCGGAGGGAGGCCCG 1081
            AGATGTGGTGGACTGGCTGTACCACAATGTGGAAGGCTTCACGGACCGGAGGGAGGCCCG
Sbjct:  663 AGATGTGGTGGACTGGCTGTACCACAATGTGGAAGGCTTCACGGACCGGAGGGAGGCCCG 722

Query: 1082 CAAGTATGCCAGCAACCTGCTGAAAGCTGGCTTCATCCGCCATACCGTCAACAAGATCAC 1141
            CAAGTATGCCAGCAACCTGCTGAAAGCTGGCTTCATCCGCCATACCGTCAACAAGATCAC
Sbjct:  723 CAAGTATGCCAGCAACCTGCTGAAAGCTGGCTTCATCCGCCATACCGTCAACAAGATCAC 782

Query: 1142 CTTCTCCGAGCAGTGCTACTACATCTTCGGTGACCTCTGCGGCAACATGGCCAACCTGTC 1201
            CTTCTCCGAGCAGTGCTACTACATCTTCGGTGACCTCTGCGGCAACATGGCCAACCTGTC
Sbjct:  783 CTTCTCCGAGCAGTGCTACTACATCTTCGGTGACCTCTGCGGCAACATGGCCAACCTGTC 842

Query: 1202 TCTCCACGATCACGATGGCTCCAGTGGCGCCT 1233
            TCTCCACGATCACGATG CTCC GTGG GCCT
Sbjct:  843 TCTCCACGATCACGATGCCTCC-GTGG-GCCT 872


>s3aq:220118872 , 474 bp.
          Length = 474

  Minus Strand HSPs:

 Score = 2340 (351.1 bits), Expect = 5.4e-100, P = 5.4e-100
 Identities = 470/473 (99%), Positives = 470/473 (99%), Strand = Minus / Plus

Query: 1959 TGGATTTAGTTCCTTTTATTTCCCTTTCAGGTACCAGACAAAGTAAAAAAGACGGACGGA 1900
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:    1 TGGATTTAGTTCCTTTTATTTCCCTTTCAGGTACCAGACAAAGTAAAAAAGACGGACGGA 60

Query: 1899 TGGAGAGAGGAACGCAGCCGGCTGGGGTGGGAGCGGAATGGAGCTGGGGGAGGGGCCCTG 1840
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   61 TGGAGAGAGGAACGCAGCCGGCTGGGGTGGGAGCGGAATGGAGCTGGGGGAGGGGCCCTG 120

Query: 1839 CTCACATCACATCCACAAAGAACTCACTGGGGTTTCCCATGGCCATGCGGAAGGACTGTC 1780
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:  121 CTCACATCACATCCACAAAGAACTCACTGGGGTTTCCCATGGCCATGCGGAAGGACTGTC 180

Query: 1779 TGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGTCGCGGCCCGGAGGGGCTCCTGGGG 1720
```

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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   181 TGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGTCGCGGCCCGGAGGGGCTCCTGGGG 240

Query:  1719 GCCCCATGGCCGCGGGCGGCGGGGGCATCATCAGCATGGGGGGGCCGTAGAGAGGGGGCA 1660
                ||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||
Sbjct:   241 GCCCCATGGCCGCGGGCGGCGGGGGCATCATCAGCATGGGGGGGCCGTAGANAGGGGGCA 300

Query:  1659 CTCCGGGAGGACCGTAGCTCGGGTGTGTGTGGTGGCTGCGAAGGCTGCTGGCCAGGGAAT 1600
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   301 CTCCGGGAGGACCGTAGCTCGGGTGTGTGTGGTGGCTGCGAAGGCTGCTGGCCAGGGAAT 360

Query:  1599 GGTGGCTGCGGTGGCTGTGCTCGCTGGCCGCCGGCCCTGAGCGCTCGCTGGGCGCCCGCT 1540
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   361 GGTGGCTGCGGTGGCTGTGCTCGCTGGCCGCCGGCCCTGAGCGCTCGCTGGGCGCCCGCT 420

Query:  1539 CCCGCGGCCCCCCGCAGGCTGCTGCGTGTGGTGTGGTCCGATTCGCTGCCGCTG 1487
                ||||||| ||||||||||||||||||||||||||||||||||||||||| |||||
Sbjct:   421 CCCGCGGACCCCGCAGGCTGCTGCGTGTGGTGTGGTCCGATTCGCTGTCGCTG 473


>s3aq:220119337 , 373 bp.
           Length = 373

  Minus Strand HSPs:

 Score = 1849 (277.4 bits), Expect = 1.0e-77, P = 1.0e-77
 Identities = 371/373 (99%), Positives = 371/373 (99%), Strand = Minus / Plus

Query:  1948 CCTTTTATTTCCCTTTCAGGTACCAGACAAAGTAAAAAAGACGGACGGATGGAGAGAGGA 1889
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:     1 CCTTTTATTTCCCTTTCAGGTACCAGACAAAGTAAAAAAGACGGACGGATGGAGAGAGGA 60

Query:  1888 ACGCAGCCGGCTGGGGTGGGAGCGGAATGGAGCTGGGGGAGGGGCCCTGCTCACATCACA 1829
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:    61 ACGCAGCCGGCTGGGGTGGGAGCGGAATGGAGCTGGGGGAGGGGCCCTGCTCACATCACA 120

Query:  1828 TCCACAAAGAACTCACTGGGGTTTCCCATGGCCATGCGGAAGGACTGTCTGCTGGCGGTC 1769
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   121 TCCACAAAGAACTCACTGGGGTTTCCCATGGCCATGCGGAAGGACTGTCTGCTGGCGGTC 180

Query:  1768 AGTTCCGGGGGCACTGAGGCCAGGTCGCGGCCCGGAGGGGCTCCTGGGGGCCCCATGGCC 1709
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   181 AGTTCCGGGGGCACTGAGGCCAGGTCGCGGCCCGGAGGGGCTCCTGGGGGCCCCATGGCC 240

Query:  1708 GCGGGCGGCGGGGGCATCATCAGCATGGGGGGGCCGTAGAGAGGGGGCACTCCGGGAGGA 1649
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct:   241 GCGGGCGGCGGGGGCATCATCAGCATGGGGGGGCCGTAGAGAGGGGGCACTCCGGGAGGA 300

Query:  1648 CCGTAGCTCGGGTGTGTGTGGTGGCTGCGAAGGCTGCTGGCCAGGGAATGGTGGCTGCGG 1589
                ||||||||||||||||||||||||||||||||||||||||| |||||||||||||| |
Sbjct:   301 CCGTAGCTCGGGTGTGTGTGGTGGCTGCGAAGGCTGCTGGCCAAGGAATGGTGGCTGCNG 360

Query:  1588 TGGCTGTGCTCGC 1576
                ||||||||||||
Sbjct:   361 TGGCTGTGCTCGC 373
```

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>s3aq:220119235 , 625 bp.
          Length = 625

  Minus Strand HSPs:

 Score = 1695 (254.3 bits), Expect = 5.6e-71, P = 5.6e-71
 Identities = 415/466 (89%), Positives = 415/466 (89%), Strand = Minus / Plus

Query:  1611 TGGCCA-G-GGAATGG-TGGCTGC-GGTGG-CTGTGCTCGCTGGCCGCCG-GCCCTGAGC 1558
             TGGCCA G GGAA G  TG CTGC GG GG C GT C CG  GGC  C G G CC G  C
Sbjct:   160 TGGCCATGCGGAAGGACTGTCTGCTGGCGGTCAGTTC-CGGGGGCA-CTGAGGCCAGGTC 217

Query:  1557 GCTCGCTGGGCGCCCGCTCCCGCGGCCCCCGCAGGCTGCTGCGTGTGGTGTGGTCCGATT 1498
             GC   C GG  G   GCTCC G GG CCCC   GGC GCTGCGTGTGGTGTGGTCCGATT
Sbjct:   218 GCGGCCCGGTAGGG-GCTCCTGGGGGCCCCAT-GGC-GCTGCGTGTGGTGTGGTCCGATT 274

Query:  1497 CGCTGCCGCTGCCCCCGGACTTGGAGTCCCCGGCCTTCGGGTCCTTCTCCTTCCTCCGAT 1438
             CGCTGCCGCTGCCCCCGGACTTGGAGTCCCCGGCCTTCGGGTCCTTCTCCTTCCTCCGAT
Sbjct:   275 CGCTGCCGCTGCCCCCGGACTTGGAGTCCCCGGCCTTCGGGTCCTTCTCCTTCCTCCGAT 334

Query:  1437 CGCTGCCGCTACGGTTGGAGCCACTGCTCCGACTGCCTTCG-CTGTGCTGACTGCTGG-C 1380
             CGCTGCCGCTACGGTTGGAGCCACTGCTCCGACTGCCTTCG CTGTGCTGACTGCTGG C
Sbjct:   335 CGCTGCCGCTACGGTTGGAGCCACTGCTCCGACTGCCTTCGGCTGTGCTGACTGCTGGGC 394

Query:  1379 GCTGCCCCCGCCGTAGCTGTAGCCCAGCTCCGGGAAGCCCGGGTGCGGGTTGTATGGGTG 1320
             GCTGCCCC GCCGTAGCTGTAGCCCAGCTCCGGGAAGCCCGG TGCGGGTTGTATGGGTG
Sbjct:   395 GCTGCCCC-GCCGTAGCTGTAGCCCAGCTCCGGGAAGCCCGG-TGCGGGTTGTATGGGTG 452

Query:  1319 CGGGGGTGGCGGGTACTGGTACGGGAAAGCCATGGGCCAAGGGGCGGCCCCCGGGTGCGG 1260
             CGGGG TGGCGGGTACTGGTACGGGAAAGCCATGGGCCAAGGGGCGGCCCCCGGGTGCGG
Sbjct:   453 CGGGG-TGGCGGGTACTGGTACGGGAAAGCCATGGGCCAAGGGGCGGCCCCCGGGTGCGG 511

Query:  1259 CAAAGGGGCCAGTGTGTCCTGGTCAGAGGCGCCACTGGAGCCATCGTGATCGTGGAGAGA 1200
             CAAAGGGGCCAGTGTGTCCTGGTCAGAGGCGCCACTGGAGCCATCGTGATCGTGGAGAGA
Sbjct:   512 CAAAGGGGCCAGTGTGTCCTGGTCAGAGGCGCCACTGGAGCCATCGTGATCGTGGAGAGA 571

Query:  1199 CAGGTTGGCCATGT-TGCCGCAGAGGTCA-CCGAAGATGTAG-TAGCACTGCTCGGA 1146
             C GGTTGGCCATGT TG  G AG GG    CCG  GATG AG TAG  CT   CGGA
Sbjct:   572 CGGGTTGGCCATGTCTGT-GAAGGGGAGGGCCG--GATGGAGCTAGGTCTTTCCGGA 625

 Score = 1321 (198.2 bits), Expect = 2.3e-53, P = 2.3e-53
 Identities = 373/460 (81%), Positives = 373/460 (81%), Strand = Minus / Plus

Query:  1958 GGATTTAGTTCCTTTTATTTCCCTTTCAGGTACCAGACAAAGTAAAAAA-GACGGACGGA 1900
             GGATTTAGTTCCTTTTATTTCCCTTTCAGGTACCAGACAAAGTAAAAAA GACGGACGGA
Sbjct:     1 GGATTTAGTTCCTTTTATTTCCCTTTCAGGTACCAGACAAAGTAAAAAAAGACGGACGGA 60

Query:  1899 TGGAGAGAGGAACGCAGCCGGCTGGGGTGGGAGCGGAATGGAGCTGGGGGAGGGGCCCTG 1840
             TGGAGAGAGGAACGCAGCCGGCTGGGGTGGGAGCGGAATGGAGCTGGGGGAGGGGCCCTG
Sbjct:    61 TGGAGAGAGGAACGCAGCCGGCTGGGGTGGGAGCGGAATGGAGCTGGGGGAGGGGCCCTG 120

Query:  1839 CTCACATCACATCCACAAAGAACTCACTGGGGTTTCCCATGGCCATGCGGAAGGACTGTC 1780
             CTCACATCACATCCACAAAGAACTCACTGGGGTTTCCCATGGCCATGCGGAAGGACTGTC
Sbjct:   121 CTCACATCACATCCACAAAGAACTCACTGGGGTTTCCCATGGCCATGCGGAAGGACTGTC 180

Query:  1779 TGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGTCGCGGCCCGG-AGGGGCTCCTGGG 1721
             TGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGTCGCGGCCCGG AGGGGCTCCTGGG
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Sbjct:   181 TGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGTCGCGGCCCGGTAGGGGCTCCTGGG 240

Query:  1720 GGCCCCATGGC-C-GCGGGCGGCGGGGGCATCATCAGCATGGGGGGGCCGTAGAGAGGGG 1663
             GGCCCCATGGC C GCG G GG G GG C    TC GC TG  G  GCC   G GA   G
Sbjct:   241 GGCCCCATGGCGCTGCGTGTGGTGTGGTCCGATTC-GC-TGCCGCTGCCCCCG-GACTTG 297

Query:  1662 GCACTCCG-GGAGGACCGTAGCT-CGGGTGTGTGTGGTGGCTGCGAAGGCTGCTGGCCAG 1605
             G A TCC  GG    C G   CT C   T   T  G T GCTGC     C G TGG  AG
Sbjct:   298 G-AGTCCCCGGCCTTCGGGTCCTTCTCCTTCCTCCGATCGCTGCCGCTACGGTTGG--AG 354

Query:  1604 GGAATGGTG-G-CTGCGGT-GGCTGTGCT--C-GCTGGCCGCCGGCCCTGAGCGCTCGCT 1551
               A TG T  G CTGC  T GGCTGTGCT  C GCTGG CGC G CCC G  CG T GCT
Sbjct:   355 CCACTGCTCCGACTGCCTTCGGCTGTGCTGACTGCTGGGCGCTGCCCC-GC-CG-TAGCT 411

Query:  1550 GGGCGCCC-GCTCCCGCG-GCCCCC-GCAGGCTGC-TGCGTGTGGTGTGG 1505
             G   GCCC GCTCC G   GCCC   GC GG TG  TG GTG GG GTGG
Sbjct:   412 GTA-GCCCAGCTCCGGGAAGCCCGGTGCGGGTTGTATGGGTGCGGGGTGG 460
```

>s3aq:220120226 , 345 bp.
Length = 345

Minus Strand HSPs:

Score = 1313 (197.0 bits), Expect = 7.1e-70, Sum P(2) = 7.1e-70
Identities = 267/271 (98%), Positives = 267/271 (98%), Strand = Minus / Plus

```
Query:   496 CTCCGGCGTGGCCGCCCTCGCTGGGCAGACACCAAAGAGTCCGTCTCTGTGTCATTGTCC 437
             CTCC G G GGCCGC CTCGCTGGGCAGACACCAAAGAGTCCGTCTCTGTGTCATTGTCC
Sbjct:    76 CTCCTGGG-GGCCGCTCTCGCTGGGCAGACACCAAAGAGTCCGTCTCTGTGTCATTGTCC 134

Query:   436 AGGTTCTCCTGGCTGCCCCCACCAGCATGAGGGTGGAAGGATGGGGGTCGGGAGTCCCCG 377
             AGGTTCTCCTGGCTGCCCCCACCAGCATGAGGGTGGAAGGATGGGGGTCGGGAGTCCCCG
Sbjct:   135 AGGTTCTCCTGGCTGCCCCCACCAGCATGAGGGTGGAAGGATGGGGGTCGGGAGTCCCCG 194

Query:   376 ATGCCTCCCGTGCGCTCCATAGGTGGTGGCAGCTCCGATGGGTTATCAGCACAGAAGGGG 317
             ATGCCTCCCGTGCGCTCCATAGGTGGTGGCAGCTCCGATGGGTTATCAGCACAGAAGGGG
Sbjct:   195 ATGCCTCCCGTGCGCTCCATAGGTGGTGGCAGCTCCGATGGGTTATCAGCACAGAAGGGG 254

Query:   316 GCTGGGTCTGGGTGTGAGCCCTCAGCTGACACCAGCCAGGACACCACCCGGCCATTGAAG 257
             GCTGGGTCTGGGTGTGAGCCCTCAGCTGACACCAGCCAGGACACCACCCGGCCATTGAAG
Sbjct:   255 GCTGGGTCTGGGTGTGAGCCCTCAGCTGACACCAGCCAGGACACCACCCGGCCATTGAAG 314

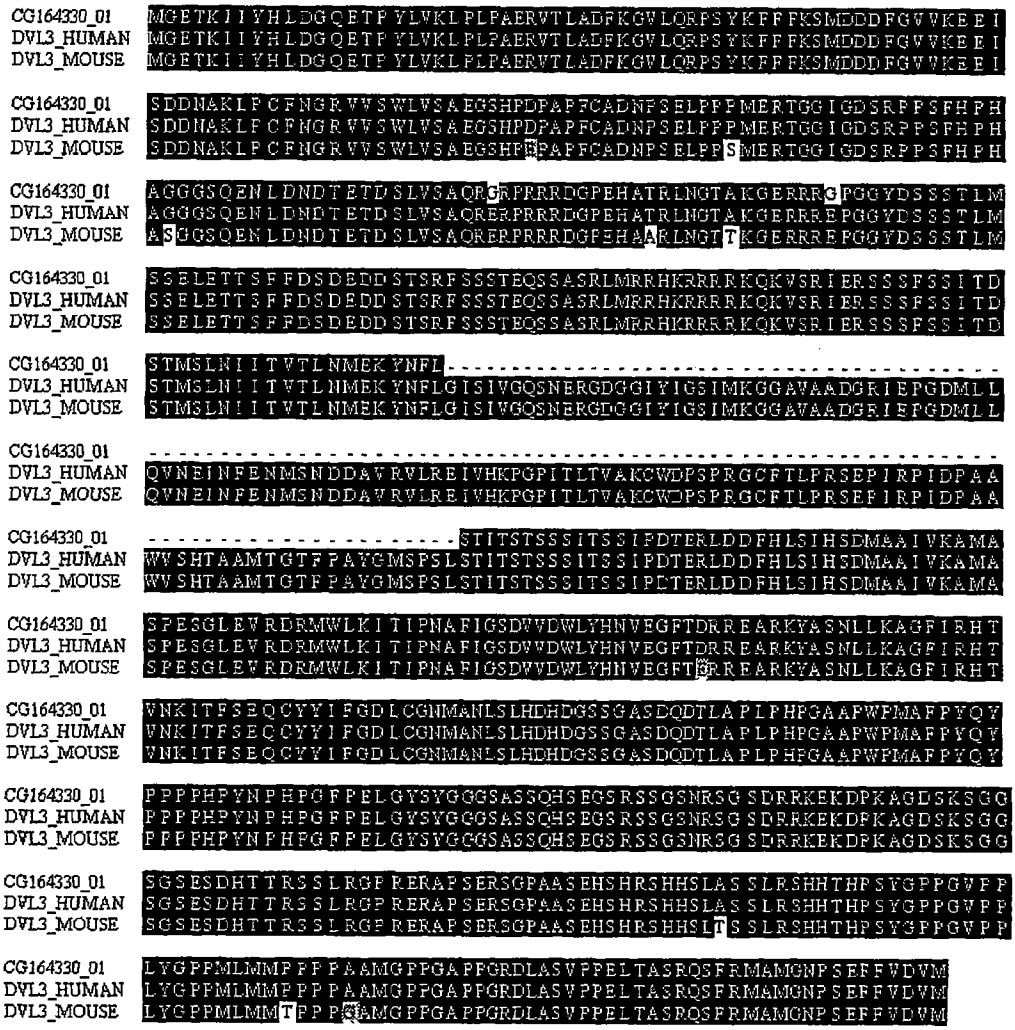
Query:   256 CATGGTAGCTTGGCATTGTCATCCGAGATCT 226
             CATGGTAGCTTGGCATTGTCATCCGAGATCT
Sbjct:   315 CATGGTAGCTTGGCATTGTCATCCGAGATCT 345
```

Score = 439 (65.9 bits), Expect = 7.1e-70, Sum P(2) = 7.1e-70
Identities = 97/103 (94%), Positives = 97/103 (94%), Strand = Minus / Plus

```
Query:  1803 CCATGGCCATGCGGAAGGACTGTCTGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGT 1744
             CCATGGCCATGCGGAAGGACTGTCTGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGT
Sbjct:     1 CCATGGCCATGCGGAAGGACTGTCTGCTGGCGGTCAGTTCCGGGGGCACTGAGGCCAGGT 60

Query:  1743 CGCGGCCCGGAGGGGCTCCTGGGGGCCCCATGGCCGC-GGGCGG 1701
             CGCGGCCCGGAGGGGCTCCTGGGGGCC C T  C GC GGGC G
Sbjct:    61 CGCGGCCCGGAGGGGCTCCTGGGGGCCGC-TCTC-GCTGGGCAG 102
```

Figure 4. ClustalW alignment of CG164330-01 protein with related proteins.



Information for the ClustalW proteins:

Accno	Common Name	Length
CG164330_01	novel Dishevelled-3-like protein	595
DVL3_HUMAN	Segment polarity protein dishevelled homolog DVL-3 (Dishevelled-3) DE (DSH homolog 3).	716
DVL3_MOUSE	Segment polarity protein dishevelled homolog DVL-3 (Dishevelled-3) DE (DSH homolog 3).	716

In the alignment shown above, black outlined amino acid residues indicate residues identically conserved between sequences (i.e., residues that may be required to preserve structural or functional properties); amino acid residues with a gray background are similar to one another

between sequences, possessing comparable physical and/or chemical properties without altering protein structure or function (e.g. the group L,V, I, and M may be considered similar); and amino acid residues with a white background are neither conserved nor similar between sequences.

Figure 5: PSORT, SignalP and hydropathy results for CuraGen Acc. No. CG164330-01.

```
                          nucleus --- Certainty=0.7000(Affirmative) < succ>
              microbody (peroxisome) --- Certainty=0.4022(Affirmative) < succ>
        mitochondrial matrix space --- Certainty=0.1000(Affirmative) < succ>
                  lysosome (lumen) --- Certainty=0.1000(Affirmative) < succ>


Is the sequence a signal peptide?
# Measure  Position  Value  Cutoff  Conclusion
  max. C    32        0.087  0.37    NO
  max. Y    39        0.053  0.34    NO
  max. S    31        0.168  0.88    NO
  mean S     1-38     0.070  0.48    NO
```